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Surveillance for Avian Influenza A(H5N1)

Mary E. Kliethermes, B.N., B.S.
Bureau of Communicable Disease Control

At the request of the Centers for Disease Control and Prevention (CDC), the Missouri Department of Health, Bureau of Communicable Disease Control has developed a state plan to perform hospital-based surveillance for influenza A(H5N1). The objective of the study is to rapidly identify an importation into the United States of influenza A(H5N1) from Asia while minimizing the disruption of existing health care delivery systems. Based on the experience in Hong Kong, hospital-based surveillance for severe illness would be an efficient and effective approach to detect the introduction of influenza A(H5N1) viruses into the United States.

Influenza A (H5N1) virus infections have been confirmed in 18 persons in Hong Kong and have caused concern among the general public, policy makers, and public health officials about the possibility for pandemic spread. Available evidence indicates that there have been two genetically different strains of A(H5N1) involved in these cases in Hong Kong and these viruses are inefficiently transmitted relative to classical human influenza viruses. Episodes of person-to-person spread or infection in laboratory workers and health care workers has not been clearly documented to date.

Influenza activity typically has two annual peaks in Hong Kong, the first during March and then a larger peak during July. Influenza activity due predominantly to influenza A (H3N2) viruses decreased during December and January in Hong Kong. While avian influenza A(H5N1) does not appear to be easily transmitted among humans, increased circulation of human influenza strains during the next few months increases the potential for reassortment between a human influenza A virus and an avian influenza A(H5N1) virus. Such a reassortment has the potential to produce a strain with antigenic characteristics for which immunity in humans does not exist. If the H5N1 virus develops the ability to be efficiently transmitted from person to person, the virus could spread worldwide very rapidly.

The Bureau of Communicable Disease Control is requesting hospitals to submit nasopharyngeal and throat swabs to the Missouri State Public Health Laboratory for viral culturing from patients who meet the criteria for screening. See criteria for screening given above.

The culture should be obtained using a cotton or Dacron swab and placed in viral transport media. The specimen should be kept cold and prepared for shipping as soon as possible. Place the specimen between refrigerant pillows in a styrofoam box and pack to prevent breakage. The pillows must be frozen when the box is packed for shipment to maintain the specimen at proper temperature.

The specimen should be shipped using a method that will facilitate delivery to the State Public Health Laboratory in the

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Criteria for Influenza A(H5N1) Screening

(Patients must meet all criteria listed below.)

- Hospitalized with unexplained pneumonia or adult respiratory distress syndrome,
- Fever (temperature >100ºF),
- Age ≥1 year and ≤60 years and
- Traveled to Asia or contact with an ill person who traveled to Asia within 10 days before onset of symptoms.

Inside this Issue...

Disease Reporting

During working hours:
Cases of reportable diseases and conditions should be reported promptly to your local health department, or to the Missouri Department of Health at **(800) 392-0272**.

Disease Emergencies:
When the reportable disease represents an emergency requiring immediate public health action, you can reach the Department of Health duty officer after hours, weekends or holidays at **(573) 751-4674**.

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shortest length of time. Address the package to Missouri State Public Health Laboratory, Attn: Mike Hanauer, Virology Unit, 307 West McCarty Street, Jefferson City, MO 65101

It is **very important** to include with the specimen the name of the submitting hospital, address, phone number and laboratory contact person; physician's name; patient's name, address and birth date; date specimen was collected; date of onset of illness; and source of specimen.

Questions regarding specimen collection, collection kits and mailing procedures should be referred to Kelly Carlson or Mike Hanauer at the Missouri State Public Health Laboratory at (573) 751-0633.

For further information on the United States hospital-based H5N1 surveillance initiative, or if you have questions regarding participation in the surveillance program, please contact Liz Kliethermes, Assistant Health Program Administrator, Bureau of Communicable Disease Control at (573) 751-6113 or (800) 392-0272.

If no resurgence of influenza A(H5N1) activity occurs in Hong Kong and no spread of influenza A(H5N1) viruses is detected outside Hong Kong, hospital-based surveillance for H5N1 viruses can be discontinued at the end of September 1998.

Pandemic Influenza Planning Exercise

Georgia Storm, R.N.
Bureau of Immunization

The Missouri Department of Health in cooperation with the State Emergency Management Agency (SEMA) sponsored a two-day exercise in February to review the Centers for Disease Control and Prevention (CDC) and the Council of State and Territorial Epidemiologists (CSTE) national planning guide for pandemic influenza. The exercise was called FLUEX '98 and was held at the State Emergency Operations Center in Jefferson City, MO. Missouri was one of five states funded by CDC to pilot test the planning guide.

Approximately 110 professionals from various state agencies, local public health agencies, nonprofit organizations and other health and emergency organizations participated in FLUEX '98.

The agenda for the first day included background information on the history of influenza epidemics, the challenges an influenza pandemic would pose, influenza microbiology and epidemiology and descriptions of how SEMA and the Federal Emergency Management Agency (FEMA) operate and what services they provide. Ray Strikas, M.D., Chief of Adult Immunization, National Immunization Program, CDC presented an overview of the national pandemic influenza plan.

A tabletop exercise was held on the second day. Participants were divided into four groups, each group representing a different area of the state. Each group was asked to review the four sections of the national planning guide:

- Laboratory and Disease-Based Surveillance
- Vaccine Delivery
- Communications
- Coordination and Emergency Preparedness and Response

After the review, groups presented their comments on the usefulness of the national guide and suggestions for change.

Missouri's response to the national pandemic influenza plan was presented to CDC and CSTE representatives at a meeting held in Atlanta on April 7–8. Recommendations for change to the national plan were made in response to comments received at that meeting.

Information gathered from FLUEX '98 will be used to plan for an influenza pandemic in Missouri. The Department of Health plans to review its Emergency Response Plan and make necessary revisions to reference and incorporate the pandemic influenza planning guide. SEMA will coordinate a review of the state's all-hazards plan and make any necessary revisions to address an influenza pandemic.

Influenza

For those of you wishing to bookmark an Internet site for the most current influenza information from the Centers for Disease Control and Prevention (CDC), try:

http://www.cdc.gov/ncidod/diseases/fluvirus.htm

This site includes the most recent CDC surveillance reports and information on antivirals for influenza A, vaccines, international trends, and the emergent influenza A(H5N1) viruses recently isolated in Hong Kong.

Missouri Department of HEALTH

Mel Carnahan
Governor

Maureen E. Dempsey, M.D.
Director

P.O. Box 570, Jefferson City, MO 65102-0570 • 573-751-6400 • FAX 573-751-6010

Dear Doctor:

Tuberculosis increased in Missouri by 10.7% during 1997 and we need your help in controlling this disease and working toward its elimination in this state by the year 2010. The Missouri Department of Health's Bureau of Tuberculosis Control needs your help in the following ways:

- Educate your patients about a strategy called directly observed therapy (DOT). DOT is a strategy that is used to ensure that patients take their tuberculosis (TB) medications as prescribed and complete their six months of treatment. Health professionals and non-health professionals can be trained to conduct DOT by simply watching a patient swallow their pills. You can think of this as a reminder system or buddy system since most people are not compliant with taking medications for such a long period of time.

  Work with your local health department to ensure that your patients are directly observed taking their TB medications. Our first priority is to have the patient go to the local health department to receive DOT for active disease. However, if a patient cannot travel to the local health department for this service, then the local health department and you might be able to identify someone else who can conduct DOT. Other possible sources include family members, friends, neighbors, or other community members such as local ministers, pharmacists, staff in physician offices, retired persons, nurses in schools and others.

  The medication dosage can be adjusted so that patients can be directly observed twice a week instead of daily.

  DOT has been adopted as the standard of care in Missouri. The use of this strategy also is recommended by the Centers for Disease Control and Prevention (CDC) in Atlanta. Areas of the country that have fully embraced DOT have witnessed significant decreases in active disease cases. These areas include Baltimore, Maryland; Fort Worth, Texas; New York City; and the state of Mississippi.

- Areas of Missouri that do not have many, or any, active disease patients should turn their attention to directly observing those patients who are TB infected without disease. This is called directly observed preventive therapy (DOPT). It's better to begin this process slowly and not become overwhelmed since more patients have TB infection than TB disease.

- Utilize four TB medications initially in treating active disease. The four TB medications that are recommended are isoniazid, rifampin, pyrazinamide and ethambutol. The use of ethambutol can be thought of as an insurance policy in terms of blocking or preventing rifampin resistance.

Your assistance with using four TB medications initially for active disease plus encouraging and educating patients about DOT/DOPT will make a difference and have an impact on this disease. If you have any questions, please call the Bureau of Tuberculosis Control at (573) 751-6122 or your local health department. Your help is very much appreciated.

Sincerely,

Vic Tomlinson
Chief
Section of Vaccine Preventable and Tuberculosis Disease Elimination

This letter was mailed in April to Missouri pulmonologists, infectious disease physicians and those in the TB diagnostic services program. All physicians who treat TB are encouraged to use directly observed therapy, the state of the art method for decreasing transmission of TB and assuring better clinical benefits.

Syphilis Outbreak in the Missouri Bootheel

Office of Epidemiology
Bureau of STD/HIV Prevention

The Bootheel region* of southeastern Missouri is currently experiencing an outbreak of syphilis. From January 1997 through April 15, 1998, 79 cases of early syphilis§ have been reported from this seven county area; 34 (43.0%) of these cases have been reported in the first 3½ months of this year. Demographic characteristics of cases reported in 1997 and through April 15, 1998, are summarized in Table 1. The majority of the cases (83.5%) have been in African Americans, but cases in whites are also occurring. The location of early syphilis cases reported since January 1, 1998, in southeast Missouri is shown in Figures 1 and 2. Almost half (47.1%) of these cases, have been from Scott County, with most being from the Sikeston area.

* Butler, Dunklin, Mississippi, New Madrid, Pemiscot, Scott, and Stoddard Counties.

§ Primary, secondary, and early latent (less than one year duration) syphilis.

Table 1. P&S and Early Latent Syphilis Cases by Gender, Race and Age Group, Missouri Bootheel*, Reported in 1997 and Through April 15, 1998

	P&S SYPHILIS				EARLY LATENT SYPHILIS			
	REPORTED 1997		REPORTED 1998**		REPORTED 1997		REPORTED 1998**	
GENDER								
MALES	6	50.0%	7	70.0%	12	36.4%	12	50.0%
FEMALES	6	50.0%	3	30.0%	21	63.6%	12	50.0%
RACE								
WHITE	1	8.3%	1	10.0%	4	12.1%	6	25.0%
BLACK	11	91.7%	9	90.0%	28	84.8%	18	75.0%
UNKNOWN	0	0.0%	0	0.0%	1	3.0%	0	0.0%
RACE AND GENDER								
WHITE MALES	0	0.0%	1	10.0%	0	0.0%	1	4.2%
BLACK MALES	6	50.0%	6	60.0%	11	33.3%	11	45.8%
UNKNOWN MALES	0	0.0%	0	0.0%	1	3.0%	0	0.0%
WHITE FEMALES	1	8.3%	0	0.0%	4	12.1%	5	20.8%
BLACK FEMALES	5	41.7%	3	30.0%	17	51.5%	7	29.2%
UNKNOWN FEMALES	0	0.0%	0	0.0%	0	0.0%	0	0.0%
AGE GROUP								
15–19	0	0.0%	0	0.0%	4	12.1%	7	29.2%
20–24	4	33.3%	4	40.0%	6	18.2%	8	33.3%
25–29	1	8.3%	2	20.0%	6	18.2%	3	12.5%
30–34	3	25.0%	1	10.0%	4	12.1%	2	8.3%
35–39	1	8.3%	1	10.0%	3	9.1%	1	4.2%
40+	3	25.0%	2	20.0%	10	30.3%	3	12.5%
TOTAL	**12**		**10**		**33**		**24**	

* Butler, Dunklin, Mississippi, New Madrid, Pemiscot, Scott and Stoddard Counties
** Through April 15, 1998

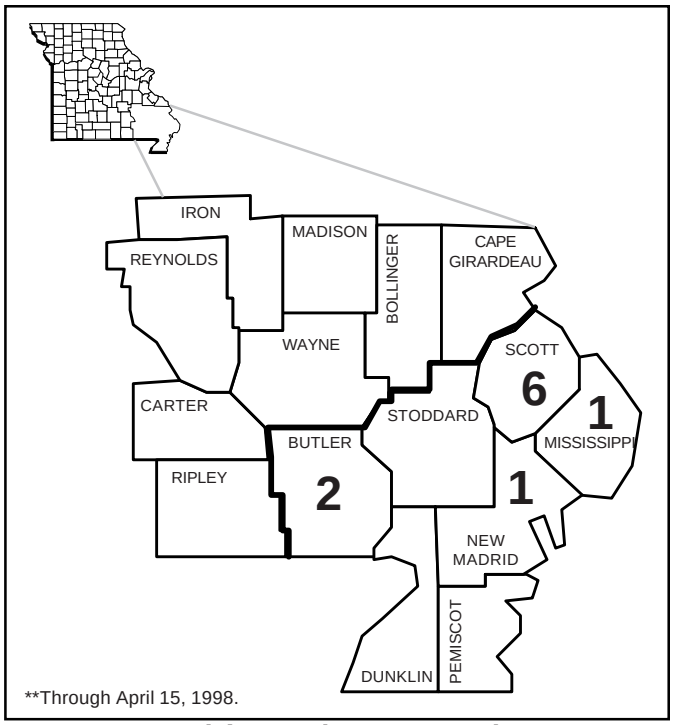

Figure 1. P&S syphilis cases by county, Southeast Missouri, 1998**

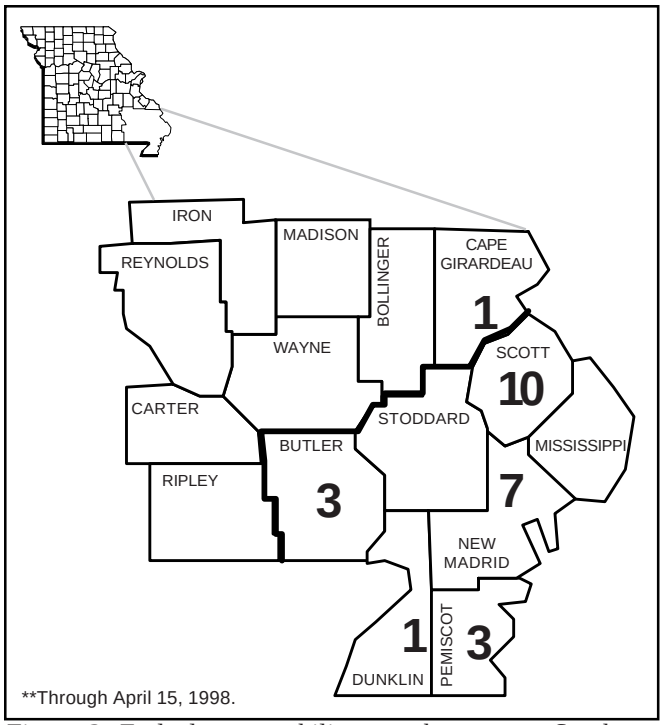

Figure 2. Early latent syphilis cases by county, Southeast Missouri, 1998**

Syphilis is a disease of particular concern because of the severe damage it can cause in infected fetuses and congenitally infected infants, and in persons with neurosyphilis and with late stage manifestations that may involve multiple organ systems. In addition, it is clear that the presence of genital ulcers such as those caused by syphilis enhance by several fold the efficiency of sexual transmission of HIV.[1,2] Fortunately, syphilis can be effectively treated with antibiotics, and if it is diagnosed in a timely manner, severe disease manifestations can be prevented.

It is important for medical providers to report all cases of syphilis immediately to the local health department, or to the Missouri Department of Health at (573) 751-6463. Prompt reporting allows specially trained public health outreach workers to offer timely assistance with partner elicitation and notification services, maximizing the opportunity to locate and treat additional infected persons, and prevent further transmission from occurring. (Reporting of syphilis cases is required by Missouri law.)

All medical providers need to be aware of the possibility of syphilis and other sexually transmitted diseases (STDs) in their patients. It is important to perform an appropriate sexual history and STD risk assessment on patients, which may include questions about illicit drug use and exchange of sex for money or drugs. Evaluation of a patient for STDs clearly requires a careful physical examination that includes examination of the skin (including the palms, soles, and flexor surfaces of the forearms), mouth, pharynx, and lymph nodes, as well as the genital area (including a pelvic exam in females) and the perineum and anal area. Patients suspected of having syphilis should have a neurological exam, remembering that central nervous system disease can occur during any stage of syphilis. Evaluation of infants and children suspected of having congenital syphilis should be according to current Centers for Disease Control and Prevention (CDC) guidelines (see below).

Certain features of syphilis can be associated with delays in diagnosis. Syphilis has manifold manifestations, and its presentation can be subtle. If the clinician is not alert, the diagnosis could be missed. In addition, early syphilis symptoms tend to be mild and painless, and as a result, the individual may not seek medical care. (However, because of the painless nature of the lesions, the person may continue to engage in sexual activity that can expose others to infection.)

Management of syphilis and other STDs is described in detail in the new CDC STD treatment guidelines.[3] The sections of these guidelines which address genital ulcer diseases and congenital syphilis are reprinted elsewhere in this issue.[†] The following points regarding syphilis diagnosis and treatment should be emphasized:

- In a patient with genital ulcer disease, a diagnosis based only on the medical history and physical examination often is inaccurate. Therefore, evaluation of all patients who have genital ulcers should include a serologic test for syphilis (RPR or VDRL) and diagnostic evaluation for herpes. (It is also strongly recommended that appropriate tests for gonorrhea, chlamydial infection, and HIV infection be performed, remembering that persons with any of these infections may not have evident signs or symptoms of disease.) Testing for HIV infection should definitely be offered to all patients diagnosed with syphilis.

- If a patient presents with a genital ulcer and has a negative nontreponemal test for syphilis (RPR, VDRL), the possibility that this represents a false-negative test result should be considered. It is important to remember that the sensitivity of nontreponemal tests varies with the levels of antibodies present during the different stages of disease. In early primary syphilis, when antibody levels may be too low to detect, results may be nonreactive, and the sensitivity of nontreponemal tests is 62–76%. Antibody levels rise as the disease progresses; titers usually peak during secondary syphilis, when the sensitivity of nontreponemal tests approaches 100%.[4]

- Parenteral penicillin G is the preferred drug for treatment of all stages of syphilis, and is the only therapy with documented efficacy for syphilis during pregnancy or for neurosyphilis. The CDC guidelines state that pregnant patients who are allergic to penicillin should be desensitized, if necessary, and treated with penicillin. Patients with neurosyphilis who report being allergic to penicillin should either be desensitized to penicillin or be managed in consultation with an expert.

- Following treatment for primary and secondary syphilis, patients should be reexamined clinically and serologically at both 6 months and 12 months; more frequent evaluation may be prudent if follow-up is uncertain. Following treatment for latent syphilis, patients should be reexamined clinically and serologically at 6, 12, and 24 months.

Appropriate evaluation and treatment of a syphilis patient's sex partner(s) is important for the partner(s) as well as for preventing further spread of infection to others, including preventing the index patient from potentially becoming reinfected. Current CDC recommendations for management of sexual contacts state that persons exposed sexually to a patient who has syphilis in any stage should be evaluated clinically and serologically as follows:

- Persons who were exposed within the 90 days preceding the diagnosis of

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[†] See pages 7 to 26. The sections from the CDC guidelines which address diseases characterized by urethritis and cervicitis (such as gonorrhea and chlamydial infections) were reprinted in the January-February 1998 issue of the *Missouri Epidemiologist*. The complete 1998 CDC STD treatment guidelines are available on the World Wide Web at http://www.cdc.gov/nchstp/dstd/dstdp.html.

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primary, secondary, or early latent syphilis in a sex partner might be infected even if seronegative; therefore, such persons should be treated presumptively.

- Persons who were exposed >90 days before the diagnosis of primary, secondary, or early latent syphilis in a sex partner should be treated presumptively if serologic test results are not available immediately and the opportunity for follow-up is uncertain.
- For purposes of partner notification and presumptive treatment of exposed sex partners, patients with syphilis of unknown duration who have high nontreponemal serologic test titers (i.e., ≥1:32) may be considered as having early syphilis. (However, serologic titers should not be used to differentiate early from late latent syphilis for the purpose of determining treatment.)

Since January 1997, no cases of congenital syphilis have been reported from the Bootheel region. However, the outbreak of early syphilis in this area indicates that the potential for congenital syphilis cases is definitely present. Medical providers who care for pregnant women are required by Missouri law to obtain, with the consent of the patient, a serologic test for syphilis on each pregnant woman at, or within 20 days of, her first visit for prenatal care. Because of the syphilis outbreak in southeast Missouri, and the continuing occurrence of syphilis in the St. Louis region, the Missouri Department of Health is currently recommending that providers in these areas perform additional serologic testing (and a repeat sexual history) twice during the third trimester: at 28 weeks of gestation and at delivery. No infant should leave the hospital without the maternal serologic status having been documented at least once during pregnancy. Any woman who delivers a stillborn infant after 20 weeks of gestation should be tested for syphilis. Also, it is especially important that all pregnant women who have syphilis undergo voluntary testing for HIV infection.[††]

Medical providers should remain up-to-date on the epidemiology, diagnosis, and treatment of syphilis and other STDs. Physicians, nurses, and other health professionals in Missouri who care for patients with STDs have access to a variety of training opportunities offered through the St. Louis STD/HIV Prevention Training Center. Information on upcoming courses can be obtained by calling (314) 747-0294, faxing (314) 362-1872, or visiting the Center's web site at http://www.umsl.edu/services/itc/std_ptc.html. Clinically oriented educational materials are available on the National STD/HIV Prevention and Training Center Network web site at http://129.137.232.101/stdptc.html (see "Educational Resources").

Finally, local and state public health officials have developed a three-part plan to address the current syphilis outbreak in the Bootheel region, and to help prevent the recurrence of the disease in this area in the future. The components of the plan are:

1. Immediate outbreak response, which includes investigation of syphilis cases and contacts, medical evaluation and presumptive treatment of contacts, syphilis screening projects in high risk populations, and provision of appropriate education to at-risk groups and to the general public.
2. Meetings between local health departments and clinical partners to improve diagnosis, treatment, reporting, follow-up and prevention of syphilis (and other STDs).
3. Meetings between public health officials and community members to identify and help implement mechanisms to improve the health of the community.

Conclusion

Since 1992, when a significant syphilis outbreak involving almost 200 reported cases occurred in the Bootheel region, there has been concern about a possible reemergence of the disease in this area. The present outbreak indicates that this concern was justified. Health care providers play a vital role in preventing the occurrence of syphilis and other STDs through appropriate evaluation, diagnosis, treatment, reporting, and follow-up practices. All patients engaging in high risk sexual behaviors should be provided education and counseling. Through the cooperative efforts of private medical providers, public health officials, and other concerned persons in the community, outbreaks of diseases such as syphilis can be effectively controlled.

REFERENCES

1. Vermund SH. Transmission of HIV-1 among adolescents and adults, in DeVita VT, et al, eds. AIDS: Biology, Diagnosis, Treatment and Prevention (4th Ed);Philadelphia: Lippincott-Raven, 1997.
2. Royce RA, et al. Sexual transmission of HIV. N Engl J Med 1997;336:1072–78.
3. CDC. 1998 Guidelines for treatment of sexually transmitted diseases. MMWR 1998;47(No. RR-1):18, 28–49.
4. U.S. Preventive Services Task Force. Guide to Clinical Preventive Services (2nd Ed), 1996:288.
5. Missouri Department of Health Policy to Reduce the Risk of Perinatal HIV Transmission in Missouri. Missouri Epidemiologist 1996;18(2):1–4.

[††] DOH has recommended that prenatal care for **all** women should routinely include HIV education and counseling, and each pregnant woman should be encouraged to undergo voluntary HIV testing. HIV education, counseling and voluntary testing should be offered at the initial prenatal visit. Uninfected pregnant women who continue to practice high-risk behaviors (e.g., injecting-drug use and/or unprotected sexual contact with an HIV-infected or high-risk partner) should be encouraged and assisted to avoid further exposure to HIV, and to be retested for HIV in the third trimester of pregnancy.[5]

1998 Guidelines for Treatment of Sexually Transmitted Diseases

(Continued from the January-February 1998 issue of the *Missouri Epidemiologist*)

Physicians and other health-care providers have a critical role in preventing and treating sexually transmitted diseases (STDs). The following recommendations for the treatment of STDs, which were developed by the Centers for Disease Control and Prevention (CDC) in consultation with a group of outside experts, are intended to assist with that effort.

The recommendations, which update those released by CDC in 1993, were reprinted from CDC's *Morbidity and Mortality Weekly Report (MMWR) Recommendations and Reports*, Vol. 47, No. RR-1, January 23, 1998. This issue of the *Missouri Epidemiologist* contains those sections of the guidelines which relate to diseases characterized by genital ulcers and congenital syphilis. Those sections relating to diseases characterized by urethritis and cervicitis were reprinted in the January-February 1998 issue. A full copy of the guidelines in pdf format can be found on the Missouri Department of Health (DOH) Home Page at **http://www.health.state.mo.us/cgi-bin/uncgi/ShowPDF?DocumentName=1998+STD+TreatmentGuide&DocumentSource=STDGuide** and also on CDC's Division of STD Prevention Home Page at **http://www.cdc.gov/nchstp/dstd/dstdp.html**.

If you have questions regarding these guidelines, please contact DOH's Bureau of STD/HIV Prevention at (573) 751-6141.

Additional information for medical providers on STDs and STD training courses is available on the Internet at the following sites:

CDC's Division of STD Prevention:
http://www.cdc.gov/nchstp/dstd/dstdp.html

CDC's Division of AIDS, STD, and TB Laboratory Research:
http://www.cdc.gov/ncidod/dastlr/dastlr.html

National Network of STD/HIV Prevention Training Centers:
http://129.137.232.101/STDPTC.html

St. Louis STD/HIV Prevention Training Center:
http://www.umsl.edu/services/itc/std_ptc.html
Ph: (314) 747-0294 or 747-1522

Medline - National Library of Medicine:
http://igm.nlm.nih.gov/

Diseases Characterized by Genital Ulcers

Congenital Syphilis

Diseases Characterized by Genital Ulcers

MANAGEMENT OF PATIENTS WHO HAVE GENITAL ULCERS

In the United States, most young, sexually active patients who have genital ulcers have either genital herpes, syphilis, or chancroid. The relative frequency of each differs by geographic area and patient population; however, in most areas of the United States, genital herpes is the most prevalent of these diseases. More than one of these diseases could be present in a patient who has genital ulcers. Each disease has been associated with an increased risk for HIV infection.

A diagnosis based only on the patient's medical history and physical examination often is inaccurate. Therefore, evaluation of all patients who have genital ulcers should include a serologic test for syphilis and diagnostic evaluation for herpes. Although, ideally, all of these tests should be conducted for each patient who has a genital ulcer, use of such tests (other than a serologic test for syphilis) may be based on test availability and clinical or epidemiologic suspicion. Specific tests for the evaluation of genital ulcers include the following:

- Darkfield examination or direct immunofluorescence test for *Treponema pallidum*,
- Culture or antigen test for herpes simplex virus (HSV), and
- Culture for *Haemophilus ducreyi*.

Polymerase chain reaction (PCR) tests for these organisms might become available commercially.

HIV testing should be
a) performed in the management of patients who have genital ulcers caused by *T. pallidum* or *H. ducreyi* and
b) considered for those who have ulcers caused by HSV
(see sections on Syphilis and Genital Herpes).

A health-care provider often must treat a patient before test results are available. In such a circumstance, the clinician should treat for the diagnosis considered most likely. If the diagnosis is unclear, many experts recommend treatment for syphilis, or for both syphilis and chancroid if the patient resides in a community in which *H. ducreyi* is a significant cause of genital ulcers, especially when diagnostic capabilities for chancroid or syphilis are not ideal. However, even after complete diagnostic evaluation, at least 25% of patients who have genital ulcers have no laboratory-confirmed diagnosis.

CHANCROID

Chancroid is endemic in some areas of the United States, and the disease also occurs in discrete outbreaks. Chancroid is a cofactor for HIV transmission, and high rates of HIV infection among patients who have chancroid have been reported in the United States and other countries. An estimated 10% of patients who have chancroid could be coinfected with *T. pallidum* or HSV.

A definitive diagnosis of chancroid requires identification of *H. ducreyi* on special culture media that are not widely available from commercial sources; even using these media, sensitivity is ≤80%. A probable diagnosis, for both clinical and surveillance purposes, may be made if the following criteria are met: a) the patient has one or more painful genital ulcers; b) the patient has no evidence of *T. pallidum* infection by darkfield examination of ulcer exudate or by a serologic test for syphilis performed at least 7 days after onset of ulcers; and c) the clinical presentation, appearance of genital ulcers, and regional lymphadenopathy, if present, are typical for chancroid and a test for HSV is negative. The combination of a painful ulcer and tender inguinal adenopathy, which occurs among one third of patients, suggests a diagnosis of chancroid; when accompanied by suppurative inguinal adenopathy, these signs are almost pathognomonic. PCR testing for *H. ducreyi* might become available soon.

Treatment

Successful treatment for chancroid cures the infection, resolves the clinical symptoms, and prevents transmission to others. In extensive cases, scarring can result despite successful therapy.

Recommended Regimens

Azithromycin 1 g orally in a single dose,

OR

Ceftriaxone 250 mg intramuscularly (IM) in a single dose,

OR

Ciprofloxacin 500 mg orally twice a day for 3 days,

OR

Erythromycin base 500 mg orally four times a day for 7 days.

NOTE: Ciprofloxacin is contraindicated for pregnant and lactating women and for persons aged <18 years.

All four regimens are effective for treatment of chancroid in HIV-infected patients. Azithromycin and ceftriaxone offer the advantage of single-dose therapy. Worldwide, several isolates with intermediate resistance to either ciprofloxacin or erythromycin have been reported.

Other Management Considerations

Patients who are uncircumcised and HIV-infected patients might not respond as well to treatment as those who are circumcised or HIV-negative. Patients should be tested for HIV infection at the time chancroid is diagnosed. Patients should be retested 3 months after the diagnosis of chancroid if the initial test results for syphilis and HIV were negative.

Follow-Up

Patients should be reexamined 3–7 days after initiation of therapy. If treatment is successful, ulcers improve symptomatically within 3 days and objectively within 7 days after therapy. If no clinical improvement is evident, the clinician must consider whether a) the diagnosis is correct, b) the patient is coinfected with another STD, c) the patient is infected with HIV, d) the treatment was not taken as instructed, or e) the *H. ducreyi* strain causing the infection is resistant to the prescribed antimicrobial.

The time required for complete healing depends on the size of the ulcer; large ulcers may require >2 weeks. In addition, healing is slower for some uncircumcised men who have ulcers under the foreskin. Clinical resolution of fluctuant lymphadenopathy is slower than that of ulcers and may require drainage, even during otherwise successful therapy. Although needle aspiration of buboes is a simpler procedure, incision and drainage of buboes may be preferred because of less need for subsequent drainage procedures.

Management of Sex Partners

Sex partners of patients who have chancroid should be examined and treated, regardless of whether symptoms of the disease are present, if they had sexual contact with the patient during the 10 days preceding onset of symptoms in the patient.

Special Considerations

Pregnancy

The safety of azithromycin for pregnant and lactating women has not been established. Ciprofloxacin is contraindicated during pregnancy. No adverse effects of chancroid on pregnancy outcome or on the fetus have been reported.

HIV Infection

HIV-infected patients who have chancroid should be monitored closely. Such patients may require longer courses of therapy than those recommended for HIV-negative patients. Healing may be slower among HIV-infected patients, and treatment failures occur with any regimen. Because data are limited concerning the therapeutic efficacy of the recommended ceftriaxone and azithromycin regimens in HIV-infected patients, these regimens should be used for such patients only if follow-up can be ensured. Some experts suggest using the erythromycin 7-day regimen for treating HIV-infected persons.

GENITAL HERPES SIMPLEX VIRUS (HSV) INFECTION

Genital herpes is a recurrent, incurable viral disease. Two serotypes of HSV have been identified: HSV-1 and HSV-2. Most cases of recurrent genital herpes are caused by HSV-2. On the basis of serologic studies, genital HSV-2 infection has been diagnosed in at least 45 million persons in the United States.

Most HSV-2–infected persons have not received a diagnosis of genital herpes. Such persons have mild or unrecognized infections that shed virus intermittently in the genital tract. Some cases of first-episode genital herpes are manifested by severe disease that might require hospitalization. Many cases of genital herpes are transmitted by persons who are unaware that they have the infection or are asymptomatic when transmission occurs.

Systemic antiviral drugs partially control the symptoms and signs of herpes episodes when used to treat first clinical episodes or recurrent episodes or when used as daily suppressive therapy. However, these drugs neither eradicate latent virus nor affect the risk, frequency, or severity of recurrences after the drug is discontinued. Randomized trials indicate that three antiviral medications provide clinical benefit for genital herpes: acyclovir, valacyclovir, and famciclovir. Valacyclovir is a valine ester of acyclovir with enhanced absorption after oral administration. Famciclovir, a prodrug of penciclovir, also has high oral bioavailability. Topical therapy with acyclovir is substantially less effective than the systemic drug, and its use is discouraged. The recommended acyclovir dosing regimens for both initial and recurrent episodes reflect substantial clinical experience, expert opinion, and FDA-approved dosages.

First Clinical Episode of Genital Herpes

Management of patients with first clinical episode of genital herpes includes antiviral therapy and counseling regarding the natural history of genital herpes, sexual and perinatal transmission, and methods to reduce such transmission. Five percent to 30% of first-episode cases of genital herpes are caused by HSV-1, but clinical recurrences are much less frequent for HSV-1 than HSV-2 genital infection. Therefore, identification of the type of the infecting strain has prognostic importance and may be useful for counseling purposes.

Recommended Regimens

Acyclovir 400 mg orally three times a day for 7–10 days,

OR

Acyclovir 200 mg orally five times a day for 7–10 days,

OR

Famciclovir 250 mg orally three times a day for 7–10 days,

OR

Valacyclovir 1 g orally twice a day for 7–10 days.

NOTE: Treatment may be extended if healing is incomplete after 10 days of therapy.

Higher dosages of acyclovir (i.e., 400 mg orally five times a day) were used in treatment studies of first-episode herpes proctitis and first-episode oral infection, including stomatitis or pharyngitis. It is unclear whether these forms of mucosal infection require higher doses of acyclovir than used for genital herpes. Valacyclovir and famciclovir probably are also effective for acute HSV proctitis or oral infection, but clinical experience is lacking.

Counseling is an important aspect of managing patients who have genital herpes. Although initial counseling can be provided at the first visit, many patients benefit from learning about the chronic aspects of the disease after the acute illness subsides. Counseling of these patients should include the following:

- Patients who have genital herpes should be told about the natural history of the disease, with emphasis on the potential for recurrent episodes, asymptomatic viral shedding, and sexual transmission.
- Patients should be advised to abstain from sexual activity when lesions or prodromal symptoms are present and encouraged to inform their sex partners that they have genital herpes. The use of condoms during all sexual exposures with new or uninfected sex partners should be encouraged.
- Sexual transmission of HSV can occur during asymptomatic periods. Asymptomatic viral shedding occurs more frequently in patients who have genital HSV-2 infection than HSV-1 infection and in patients who have had genital herpes for <12 months. Such patients should be counseled to prevent spread of the infection.

- The risk for neonatal infection should be explained to all patients, including men. Childbearing-aged women who have genital herpes should be advised to inform health-care providers who care for them during pregnancy about the HSV infection.
- Patients having a first episode of genital herpes should be advised that a) episodic antiviral therapy during recurrent episodes might shorten the duration of lesions and b) suppressive antiviral therapy can ameliorate or prevent recurrent outbreaks.

Recurrent Episodes of HSV Disease

Most patients with first-episode genital HSV-2 infection will have recurrent episodes of genital lesions. Episodic or suppressive antiviral therapy might shorten the duration of lesions or ameliorate recurrences. Because many patients benefit from antiviral therapy, options for treatment should be discussed with all patients.

When treatment is started during the prodrome or within 1 day after onset of lesions, many patients who have recurrent disease benefit from episodic therapy. If episodic treatment of recurrences is chosen, the patient should be provided with antiviral therapy, or a prescription for the medication, so that treatment can be initiated at the first sign of prodrome or genital lesions.

Daily suppressive therapy reduces the frequency of genital herpes recurrences by ≥75% among patients who have frequent recurrences (i.e., six or more recurrences per year). Safety and efficacy have been documented among patients receiving daily therapy with acyclovir for as long as 6 years, and with valacyclovir and famciclovir for 1 year. Suppressive therapy has not been associated with emergence of clinically significant acyclovir resistance among immunocompetent patients. After 1 year of continuous suppressive therapy, discontinuation of therapy should be discussed with the patient to assess the patient's psychological adjustment to genital herpes and rate of recurrent episodes, as the frequency of recurrences decreases over time in many patients. Insufficient experience with famciclovir and valacyclovir prevents recommendation of these drugs for >1 year.

Suppressive treatment with acyclovir reduces but does not eliminate asymptomatic viral shedding. Therefore, the extent to which suppressive therapy may prevent HSV transmission is unknown.

Recommended Regimens for Episodic Recurrent Infection

Acyclovir 400 mg orally three times a day for 5 days,
OR
Acyclovir 200 mg orally five times a day for 5 days,
OR
Acyclovir 800 mg orally twice a day for 5 days,
OR
Famciclovir 125 mg orally twice a day for 5 days,
OR
Valacyclovir 500 mg orally twice a day for 5 days.

Recommended Regimens for Daily Suppressive Therapy

Acyclovir 400 mg orally twice a day,
OR
Famciclovir 250 mg orally twice a day,
OR
Valacyclovir 500 mg orally once a day,
OR
Valacyclovir 1,000 mg orally once a day.

Valacyclovir 500 mg once a day appears less effective than other valacyclovir dosing regimens in patients who have very frequent recurrences (i.e., ≥10 episodes per year). Few comparative studies of valacyclovir and famciclovir with acyclovir have been conducted. The results of these studies suggest that valacyclovir and famciclovir are comparable to acyclovir in clinical outcome. However, valacyclovir and famciclovir may provide increased ease in administration, which is an important consideration for prolonged treatment.

Severe Disease

IV therapy should be provided for patients who have severe disease or complications necessitating hospitalization, such as disseminated infection, pneumonitis, hepatitis, or complications of the central nervous system (e.g., meningitis or encephalitis).

Recommended Regimen
Acyclovir 5–10 mg/kg body weight IV every 8 hours for 5–7 days or until clinical resolution is attained.

Management of Sex Partners

The sex partners of patients who have genital herpes are likely to benefit from evaluation and counseling. Symptomatic sex partners should be evaluated and treated in the same manner as patients who have genital lesions. However, most persons who have genital HSV infection do not have a history of typical genital lesions. These persons and their future sex partners may benefit from evaluation and counseling. Thus, even asymptomatic sex partners of patients who have newly diagnosed genital herpes should be questioned concerning histories of typical and atypical genital lesions, and they should be encouraged to examine themselves for lesions in the future and seek medical attention promptly if lesions appear.

Most of the available HSV antibody tests do not accurately discriminate between HSV-1 and HSV-2 antibodies, and their use is not currently recommended. Sensitive and type-specific serum antibody assays may become commercially available and contribute to future intervention strategies.

Special Considerations

Allergy, Intolerance, or Adverse Reactions
Allergic and other adverse reactions to acyclovir, valacyclovir, and famciclovir are infrequent. Desensitization to acyclovir has been described previously (23).

HIV Infection
Immunocompromised patients might have prolonged and/or severe episodes of genital or perianal herpes. Lesions caused by HSV are relatively common among HIV-infected patients and may be severe, painful, and atypical. Intermittent or suppressive therapy with oral antiviral agents is often beneficial.

The dosage of antiviral drugs for HIV-infected patients is controversial, but clinical experience strongly suggests that immunocompromised patients benefit from increased doses of antiviral drugs. Regimens such as acyclovir 400 mg orally three to five times a day, as used for other immunocompromised patients, have been useful. Therapy should be continued until clinical resolution is attained. Famciclovir 500 mg twice a day has been effective in decreasing both the rate of recurrences and the rate of subclinical shedding among HIV-infected patients. In immunocompromised patients, valacyclovir in doses of 8 g per day has been associated with a syndrome resembling either hemolytic uremic syndrome or thrombotic thrombocytopenic purpura. However, in the doses recommended for treatment of genital herpes, valacyclovir, acyclovir, and famciclovir probably are safe for use in immunocompromised patients. For severe cases, acyclovir 5 mg/kg IV every 8 hours may be required.

If lesions persist in a patient receiving acyclovir treatment, resistance of the HSV strain to acyclovir should be suspected. Such patients should be managed in consultation with an expert. For severe cases caused by proven or suspected acyclovir-resistant strains, alternate therapy should be administered. All acyclovir-resistant strains are resistant to valacyclovir, and most are resistant to famciclovir. Foscarnet, 40 mg/kg body weight IV every 8 hours until clinical resolution is attained, is often effective for treatment of acyclovir-resistant genital herpes. Topical cidofovir gel 1% applied to the lesions once daily for 5 consecutive days also might be effective.

Pregnancy
The safety of systemic acyclovir and valacyclovir therapy in pregnant women has not been established. Glaxo-Wellcome, Inc., in cooperation with CDC, maintains a registry to assess the use and effects of acyclovir and valacyclovir during pregnancy. Women who receive acyclovir or valacyclovir during pregnancy should be reported to this registry; telephone (800) 722-9292, extension 38465.

Current registry findings do not indicate an increased risk for major birth defects after acyclovir treatment (i.e., in comparison with the general population). These findings provide some assurance in counseling women who have had prenatal exposure to acyclovir. The accumulated case histories represent an insufficient sample for reaching reliable and definitive conclusions regarding the risks associated with acyclovir treatment during pregnancy. Prenatal exposure to valacyclovir and famciclovir is too limited to provide useful information on pregnancy outcomes.

The first clinical episode of genital herpes during pregnancy may be treated with oral acyclovir. In the presence of life-threatening maternal HSV infection (e.g., disseminated infection, encephalitis, pneumonitis, or hepatitis), acyclovir administered IV is indicated. Investigations of acyclovir use among pregnant women suggest that acyclovir treatment near term might reduce the rate of abdominal deliveries among women who have frequently recurring or newly acquired genital herpes by decreasing the incidence of active lesions. However, routine administration of acyclovir to pregnant women who have a history of recurrent genital herpes is not recommended at this time.

Perinatal Infection

Most mothers of infants who acquire neonatal herpes lack histories of clinically evident genital herpes. The risk for transmission to the neonate from an infected mother is high among women who acquire genital herpes near the time of delivery (30%–50%) and is low among women who have a history of recurrent herpes at term and women who acquire genital HSV during the first half of pregnancy (3%). Therefore, prevention of neonatal herpes should emphasize prevention of acquisition of genital HSV infection during late pregnancy. Susceptible women whose partners have oral or genital HSV infection, or those whose sex partners' infection status is unknown, should be counseled to avoid unprotected genital and oral sexual contact during late pregnancy. The results of viral cultures during pregnancy do not predict viral shedding at the time of delivery, and such cultures are not indicated routinely.

At the onset of labor, all women should be examined and carefully questioned regarding whether they have symptoms of genital herpes. Infants of women who do not have symptoms or signs of genital herpes infection or its prodrome may be delivered vaginally. Abdominal delivery does not completely eliminate the risk for HSV infection in the neonate.

Infants exposed to HSV during birth, as proven by virus isolation or presumed by observation of lesions, should be followed carefully. Some authorities recommend that such infants undergo surveillance cultures of mucosal surfaces to detect HSV infection before development of clinical signs. Available data do not support the routine use of acyclovir for asymptomatic infants exposed during birth through an infected birth canal, because the risk for infection in most infants is low. However, infants born to women who acquired genital herpes near term are at high risk for neonatal herpes, and some experts recommend acyclovir therapy for these infants. Such pregnancies and newborns should be managed in consultation with an expert. All infants who have evidence of neonatal herpes should be promptly evaluated and treated with systemic acyclovir (19). Acyclovir 30–60 mg/kg/day for 10–21 days is the regimen of choice.

LYMPHOGRANULOMA VENEREUM

Lymphogranuloma venereum (LGV), a rare disease in the United States, is caused by the invasive serovars L1, L2, or L3 of *C. trachomatis*. The most frequent clinical manifestation of LGV among heterosexual men is tender inguinal and/or femoral lymphadenopathy that is usually unilateral. Women and homosexually active men might have proctocolitis or inflammatory involvement of perirectal or perianal lymphatic tissues that can result in fistulas and strictures. When most patients seek medical care, they no longer have the self-limited genital ulcer that sometimes occurs at the inoculation site. The diagnosis usually is made serologically and by exclusion of other causes of inguinal lymphadenopathy or genital ulcers.

Treatment

Treatment cures infection and prevents ongoing tissue damage, although tissue reaction can result in scarring. Buboes may require aspiration through intact skin or incision and drainage to prevent the formation of inguinal/femoral ulcerations. Doxycycline is the preferred treatment.

Recommended Regimen

Doxycycline 100 mg orally twice a day for 21 days.

Alternative Regimen

Erythromycin base 500 mg orally four times a day for 21 days.

The activity of azithromycin against *C. trachomatis* suggests that it may be effective in multiple doses over 2–3 weeks, but clinical data regarding its use are lacking.

Follow-Up

Patients should be followed clinically until signs and symptoms have resolved.

Management of Sex Partners

Sex partners of patients who have LGV should be examined, tested for urethral or cervical chlamydial infection, and treated if they had sexual contact with the patient during the 30 days preceding onset of symptoms in the patient.

Special Considerations

Pregnancy
Pregnant women should be treated with the erythromycin regimen.

HIV Infection
HIV-infected persons who have LGV should be treated according to the regimens cited previously. Anecdotal evidence suggests that LGV infection in HIV-positive patients may require prolonged therapy and that resolution might be delayed.

SYPHILIS

General Principles

Background

Syphilis is a systemic disease caused by *T. pallidum*. Patients who have syphilis may seek treatment for signs or symptoms of primary infection (i.e., ulcer or chancre at the infection site), secondary infection (i.e., manifestations that include rash, mucocutaneous lesions, and adenopathy), or tertiary infection (i.e., cardiac, neurologic, ophthalmic, auditory, or gummatous lesions). Infections also may be detected by serologic testing during the latent stage. Latent syphilis acquired within the preceding year is referred to as early latent syphilis; all other cases of latent syphilis are either late latent syphilis or syphilis of unknown duration. Treatment for late latent syphilis, as well as tertiary syphilis, theoretically may require a longer duration of therapy because organisms are dividing more slowly; however, the validity and importance of this concept have not been determined.

Diagnostic Considerations and Use of Serologic Tests

Darkfield examinations and direct fluorescent antibody tests of lesion exudate or tissue are the definitive methods for diagnosing early syphilis. A presumptive diagnosis is possible with the use of two types of serologic tests for syphilis: a) nontreponemal (e.g., Venereal Disease Research Laboratory [VDRL] and RPR) and b) treponemal (e.g., fluorescent treponemal antibody absorbed [FTA-ABS] and microhemagglutination assay for antibody to *T. pallidum* [MHA-TP]). The use of only one type of test is insufficient for diagnosis because false-positive nontreponemal test results occasionally occur secondary to various medical conditions. Nontreponemal test antibody titers usually correlate with disease activity, and results should be reported quantitatively. A fourfold change in titer, equivalent to a change of two dilutions (e.g., from 1:16 to 1:4 or from 1:8 to 1:32), usually is considered necessary to demonstrate a clinically significant difference between two nontreponemal test results that were obtained by using the same serologic test. It is expected that the nontreponemal test will eventually become nonreactive after treatment; however, in some patients, nontreponemal antibodies can persist at a low titer for a long period, sometimes for the remainder of their lives. This response is referred to as the serofast reaction. Most patients who have reactive treponemal tests will have reactive tests for the remainder of their lives, regardless of treatment or disease activity. However, 15%–25% of patients treated during the primary stage might revert to being serologically nonreactive after 2–3 years. Treponemal test antibody titers correlate poorly with disease activity and should not be used to assess treatment response.

Sequential serologic tests should be performed by using the same testing method (e.g., VDRL or RPR), preferably by the same laboratory. The VDRL and RPR are equally valid, but quantitative results from the two tests cannot be compared directly because RPR titers often are slightly higher than VDRL titers.

HIV-infected patients can have abnormal serologic test results (i.e., unusually high, unusually low, and fluctuating titers). For such patients with clinical syndromes suggestive of early syphilis, use of other tests (e.g., biopsy and direct microscopy) should be considered. However, for most HIV-infected patients, serologic tests appear to be accurate and reliable for the diagnosis of syphilis and for evaluation of treatment response.

No single test can be used to diagnose all cases of neurosyphilis. The diagnosis of neurosyphilis can be made based on various combinations of reactive serologic test results, abnormalities of cerebrospinal fluid (CSF) cell count or protein, or a reactive VDRL-CSF with or without clinical manifestations. The CSF leukocyte count usually is elevated (>5 WBCs/mm^3) when neurosyphilis is present, and it also is a sensitive measure of the effectiveness of therapy. The VDRL-CSF is the standard serologic test for CSF; when reactive in the absence of substantial contamination of CSF with blood, it is considered diagnostic of neurosyphilis. However, the VDRL-CSF may be nonreactive when neurosyphilis is present. Some experts recommend performing an FTA-ABS test on CSF. The CSF FTA-ABS is less specific (i.e., yields more false-positive results) for neurosyphilis than the VDRL-CSF. However, the test is believed to be highly sensitive, and some experts believe that a negative CSF FTA-ABS test excludes neurosyphilis.

Treatment

Parenteral penicillin G is the preferred drug for treatment of all stages of syphilis. The preparation(s) used (i.e., benzathine, aqueous procaine, or aqueous crystalline), the dosage, and the length of treatment depend on the stage and clinical manifestations of disease.

The efficacy of penicillin for the treatment of syphilis was well established through clinical experience before the value of randomized controlled clinical trials was recognized. Therefore, almost all the recommendations for the treatment of syphilis are based on expert opinion reinforced by case series, clinical trials, and 50 years of clinical experience.

Parenteral penicillin G is the only therapy with documented efficacy for neurosyphilis or for syphilis during pregnancy. Patients who report a penicillin allergy, including pregnant women with syphilis in any stage and patients with neurosyphilis, should be desensitized and treated with penicillin. Skin testing for penicillin allergy may be useful in some settings (see Management of Patients Who Have a History of Penicillin Allergy), because the minor determinants needed for penicillin skin testing are unavailable commercially.

The Jarisch-Herxheimer reaction is an acute febrile reaction—often accompanied by headache, myalgia, and other symptoms—that might occur within the first 24 hours after any therapy for syphilis; patients should be advised of this possible adverse reaction. The Jarisch-Herxheimer reaction often occurs among patients who have early syphilis. Antipyretics may be recommended, but no proven methods prevent this reaction. The Jarisch-Herxheimer reaction may induce early labor or cause fetal distress among pregnant women. This concern should not prevent or delay therapy (see Syphilis During Pregnancy).

Management of Sex Partners

Sexual transmission of *T. pallidum* occurs only when mucocutaneous syphilitic lesions are present; such manifestations are uncommon after the first year of infection. However, persons exposed sexually to a patient who has syphilis in any stage should be evaluated clinically and serologically according to the following recommendations:

- Persons who were exposed within the 90 days preceding the diagnosis of primary, secondary, or early latent syphilis in a sex partner might be infected even if seronegative; therefore, such persons should be treated presumptively.
- Persons who were exposed >90 days before the diagnosis of primary, secondary, or early latent syphilis in a sex partner should be treated presumptively if serologic test results are not available immediately and the opportunity for follow-up is uncertain.
- For purposes of partner notification and presumptive treatment of exposed sex partners, patients with syphilis of unknown duration who have high nontreponemal serologic test titers (i.e., ≥1:32) may be considered as having early syphilis. However, serologic titers should not be used to differentiate early from late latent syphilis for the purpose of determining treatment (see section regarding treatment of latent syphilis).
- Long-term sex partners of patients who have late syphilis should be evaluated clinically and serologically for syphilis and treated on the basis of the findings of the evaluation.

The time periods before treatment used for identifying at-risk sex partners are a) 3 months plus duration of symptoms for primary syphilis, b) 6 months plus duration of symptoms for secondary syphilis, and c) 1 year for early latent syphilis.

Primary and Secondary Syphilis

Treatment

Parenteral penicillin G has been used effectively for four decades to achieve a local cure (i.e., healing of lesions and prevention of sexual transmission) and to prevent late sequelae. However, no adequately conducted comparative trials have been performed to guide the selection of an optimal penicillin regimen (i.e., the dose, duration, and preparation). Substantially fewer data are available concerning nonpenicillin regimens.

Recommended Regimen for Adults
Patients who have primary or secondary syphilis should be treated with the following regimen:
Benzathine penicillin G 2.4 million units IM in a single dose.

NOTE: Recommendations for treating pregnant women and HIV-infected patients for syphilis are discussed in separate sections.

Recommended Regimen for Children
After the newborn period, children in whom syphilis is diagnosed should have a CSF examination to detect asymptomatic neurosyphilis, and birth and maternal medical records should be reviewed to assess whether the child has congenital or acquired syphilis (see Congenital Syphilis). Children with acquired primary or secondary syphilis should be evaluated (including consultation with child-protection services) and treated by using the following pediatric regimen (see Sexual Assault or Abuse of Children).
Benzathine penicillin G 50,000 units/kg IM, up to the adult dose of 2.4 million units in a single dose.

Other Management Considerations

All patients who have syphilis should be tested for HIV infection. In geographic areas in which the prevalence of HIV is high, patients who have primary syphilis should be retested for HIV after 3 months if the first HIV test result was negative. This recommendation will become particularly important if it can be demonstrated that intensive antiviral therapy administered soon after HIV seroconversion is beneficial.

Patients who have syphilis and who also have symptoms or signs suggesting neurologic disease (e.g., meningitis) or ophthalmic disease (e.g., uveitis) should be evaluated fully for neurosyphilis and syphilitic eye disease; this evaluation should include CSF analysis and ocular slit-lamp examination. Such patients should be treated appropriately according to the results of this evaluation.

Invasion of CSF by *T. pallidum* accompanied by CSF abnormalities is common among adults who have primary or secondary syphilis. However, neurosyphilis develops in only a few patients after treatment with the regimens described in this report. Therefore, unless clinical signs or symptoms of neurologic or ophthalmic involvement are present, lumbar puncture is not recommended for routine evaluation of patients who have primary or secondary syphilis.

Follow-Up

Treatment failures can occur with any regimen. However, assessing response to treatment often is difficult, and no definitive criteria for cure or failure have been established. Serologic test titers may decline more slowly for patients who previously had syphilis. Patients should be reexamined clinically and serologically at both 6 months and 12 months; more frequent evaluation may be prudent if follow-up is uncertain.

Patients who have signs or symptoms that persist or recur or who have a sustained fourfold increase in nontreponemal test titer (i.e., in comparison with either the baseline titer or a subsequent result) probably failed treatment or were reinfected. These patients should be retreated after reevaluation for HIV infection. Unless reinfection with *T. pallidum* is certain, a lumbar puncture also should be performed.

Failure of nontreponemal test titers to decline fourfold within 6 months after therapy for primary or secondary syphilis identifies persons at risk for treatment failure. Such persons should be reevaluated for HIV infection. Optimal management of such patients is unclear. At a minimum, these patients should have additional clinical and serologic follow-up. HIV-infected patients should be evaluated more frequently (i.e., at 3-month intervals instead of 6-month intervals). If additional follow-up cannot be ensured, re-treatment is recommended. Some experts recommend CSF examination in such situations.

When patients are retreated, most experts recommend re-treatment with three weekly injections of benzathine penicillin G 2.4 million units IM, unless CSF examination indicates that neurosyphilis is present.

Management of Sex Partners

Refer to General Principles, Management of Sex Partners.

Special Considerations

Penicillin Allergy
Nonpregnant penicillin-allergic patients who have primary or secondary syphilis should be treated with one of the following regimens. Close follow-up of such patients is essential.

Recommended Regimens

Doxycycline 100 mg orally twice a day for 2 weeks,

OR

Tetracycline 500 mg orally four times a day for 2 weeks.

There is less clinical experience with doxycycline than with tetracycline, but compliance is likely to be better with doxycycline. Therapy for a patient who cannot tolerate either doxycycline or tetracycline should depend on whether the patient's compliance with the therapy regimen and with follow-up examinations can be ensured.

Pharmacologic and bacteriologic considerations suggest that ceftriaxone should be effective, but data concerning ceftriaxone are limited and clinical experience is insufficient to enable identification of late failures. The optimal dose and duration have not been established for ceftriaxone, but a suggested daily regimen of 1 g may be considered if treponemacidal levels in the blood can be maintained for 8–10 days. Single-dose ceftriaxone therapy is not effective for treating syphilis.

For nonpregnant patients whose compliance with therapy and follow-up can be ensured, an alternative regimen is erythromycin 500 mg orally four times a day for 2 weeks. However, erythromycin is less effective than the other recommended regimens.

Patients whose compliance with therapy or follow-up cannot be ensured should be desensitized and treated with penicillin. Skin testing for penicillin allergy may be useful in some circumstances in which the reagents and expertise to perform the test adequately are available (see Management of Patients Who Have a History of Penicillin Allergy).

Pregnancy
Pregnant patients who are allergic to penicillin should be desensitized, if necessary, and treated with penicillin (see Management of Patients Who Have a History of Penicillin Allergy and Syphilis During Pregnancy).

HIV Infection
Refer to Syphilis in HIV-Infected Persons.

Latent Syphilis

Latent syphilis is defined as those periods after infection with *T. pallidum* when patients are seroreactive, but demonstrate no other evidence of disease. Patients who have latent syphilis and who acquired syphilis within the preceding year are classified as having early latent syphilis. Patients can be demonstrated as having early latent syphilis if, within the year preceding the evaluation, they had a) a documented seroconversion, b) unequivocal symptoms of primary or secondary syphilis, or c) a sex partner who had primary, secondary, or early latent syphilis. Almost all other patients have latent syphilis of unknown duration and should be managed as if they had late latent syphilis.

Nontreponemal serologic titers usually are higher during early latent syphilis than late latent syphilis. However, early latent syphilis cannot be reliably distinguished from late latent syphilis solely on the basis of nontreponemal titers. Regardless of the level of the nontreponemal titers, patients in whom the illness does not meet the definition of early syphilis should be treated as if they have late latent infection. All sexually active women with reactive nontreponemal serologic tests should have a pelvic examination before syphilis staging is completed to evaluate for internal mucosal lesions. All patients who have syphilis should be tested for HIV infection.

Treatment

Treatment of latent syphilis is intended to prevent occurrence or progression of late complications. Although clinical experience supports the effectiveness of penicillin in achieving these goals, limited evidence is available for guidance in choosing specific regimens. There is minimal evidence to support the use of nonpenicillin regimens.

Recommended Regimens for Adults

The following regimens are recommended for nonallergic patients who have normal CSF examinations (if performed):

Early Latent Syphilis:

Benzathine penicillin G 2.4 million units IM in a single dose.

Late Latent Syphilis or Latent Syphilis of Unknown Duration:

Benzathine penicillin G 7.2 million units total, administered as three doses of 2.4 million units IM each at 1-week intervals.

Recommended Regimens for Children

After the newborn period, children in whom syphilis is diagnosed should have a CSF examination to exclude neurosyphilis, and birth and maternal medical records should be reviewed to assess whether the child has congenital or acquired syphilis (see Congenital Syphilis). Older children with acquired latent syphilis should be evaluated as described for adults and treated using the following pediatric regimens (see Sexual Assault or Abuse of Children). These regimens are for nonallergic children who have acquired syphilis and whose results of the CSF examination were normal.

Early Latent Syphilis:

Benzathine penicillin G 50,000 units/kg IM, up to the adult dose of 2.4 million units in a single dose.

Late Latent Syphilis or Latent Syphilis of Unknown Duration:

Benzathine penicillin G 50,000 units/kg IM, up to the adult dose of 2.4 million units, administered as three doses at 1-week intervals (total 150,000 units/kg up to the adult total dose of 7.2 million units).

Other Management Considerations

All patients who have latent syphilis should be evaluated clinically for evidence of tertiary disease (e.g., aortitis, neurosyphilis, gumma, and iritis). Patients who have syphilis and who demonstrate any of the following criteria should have a prompt CSF examination:

- Neurologic or ophthalmic signs or symptoms;
- Evidence of active tertiary syphilis (e.g., aortitis, gumma, and iritis);
- Treatment failure; and
- HIV infection with late latent syphilis or syphilis of unknown duration.

If dictated by circumstances and patient preferences, a CSF examination may be performed for patients who do not meet these criteria. If a CSF examination is performed and the results indicate abnormalities consistent with neurosyphilis, the patient should be treated for neurosyphilis (see Neurosyphilis).

Follow-Up

Quantitative nontreponemal serologic tests should be repeated at 6, 12, and 24 months. Limited data are available to guide evaluation of the treatment response for patients who have latent syphilis. Patients should be evaluated for neurosyphilis and retreated appropriately if a) titers increase fourfold, b) an initially high titer (≥1:32) fails to decline at least fourfold (i.e., two dilutions) within 12–24 months, or c) signs or symptoms attributable to syphilis develop in the patient.

Management of Sex Partners

Refer to General Principles, Management of Sex Partners.

Special Considerations

Penicillin Allergy
Nonpregnant patients who have latent syphilis and who are allergic to penicillin should be treated with one of the following regimens.

Recommended Regimens

Doxycycline 100 mg orally twice a day,

OR

Tetracycline 500 mg orally four times a day.

Both drugs should be administered for 2 weeks if the duration of infection is known to have been <1 year; otherwise, they should be administered for 4 weeks.

Pregnancy
Pregnant patients who are allergic to penicillin should be desensitized and treated with penicillin (see Management of Patients Who Have a History of Penicillin Allergy and Syphilis During Pregnancy).

HIV Infection
Refer to Syphilis in HIV-Infected Persons.

Tertiary Syphilis

Tertiary syphilis refers to gumma and cardiovascular syphilis, but not to neurosyphilis. Nonallergic patients without evidence of neurosyphilis should be treated with the following regimen.

Recommended Regimen

Benzathine penicillin G 7.2 million units total, administered as three doses of 2.4 million units IM at 1-week intervals.

Other Management Considerations

Patients who have symptomatic late syphilis should have a CSF examination before therapy is initiated. Some experts treat all patients who have cardiovascular syphilis with a neurosyphilis regimen. The complete management of patients who have cardiovascular or gummatous syphilis is beyond the scope of these guidelines. These patients should be managed in consultation with an expert.

Follow-Up

Information is lacking with regard to follow-up of patients who have late syphilis. The clinical response depends partially on the nature of the lesions.

Management of Sex Partners

Refer to General Principles, Management of Sex Partners.

Special Considerations

Penicillin Allergy
Patients allergic to penicillin should be treated according to the recommended regimens for late latent syphilis.

Pregnancy
Pregnant patients who are allergic to penicillin should be desensitized, if necessary, and treated with penicillin (see Management of Patients Who Have a History of Penicillin Allergy and Syphilis During Pregnancy).

HIV Infection
Refer to Syphilis in HIV-Infected Persons.

Neurosyphilis

Treatment

Central nervous system disease can occur during any stage of syphilis. A patient who has clinical evidence of neurologic involvement with syphilis (e.g., ophthalmic or auditory symptoms, cranial nerve palsies, and symptoms or signs of meningitis) should have a CSF examination.

Syphilitic uveitis or other ocular manifestations frequently are associated with neurosyphilis; patients with these symptoms should be treated according to the recommendations for neurosyphilis. A CSF examination should be performed for all such patients to identify those with abnormalities who should have follow-up CSF examinations to assess treatment response.

Patients who have neurosyphilis or syphilitic eye disease (e.g., uveitis, neuroretinitis, or optic neuritis) and who are not allergic to penicillin should be treated with the following regimen:

Recommended Regimen
Aqueous crystalline penicillin G 18–24 million units a day, administered as 3–4 million units IV every 4 hours for 10–14 days.

If compliance with therapy can be ensured, patients may be treated with the following alternative regimen:

Alternative Regimen
Procaine penicillin 2.4 million units IM a day, PLUS **Probenecid** 500 mg orally four times a day, both for 10–14 days.

The durations of the recommended and alternative regimens for neurosyphilis are shorter than that of the regimen used for late syphilis in the absence of neurosyphilis. Therefore, some experts administer benzathine penicillin, 2.4 million units IM, after completion of these neurosyphilis treatment regimens to provide a comparable total duration of therapy.

Other Management Considerations

Other considerations in the management of patients who have neurosyphilis are as follows:

- All patients who have syphilis should be tested for HIV.
- Many experts recommend treating patients who have evidence of auditory disease caused by syphilis in the same manner as for neurosyphilis, regardless of the findings on CSF examination. Although systemic steroids are used frequently as adjunctive therapy for otologic syphilis, such drugs have not been proven beneficial.

Follow-Up

If CSF pleocytosis was present initially, a CSF examination should be repeated every 6 months until the cell count is normal. Follow-up CSF examinations also can be used to evaluate changes in the VDRL-CSF or CSF protein after therapy; however, changes in these two parameters are slower, and persistent abnormalities are of less importance. If the cell count has not decreased after 6 months, or if the CSF is not entirely normal after 2 years, re-treatment should be considered.

Management of Sex Partners

Refer to General Principles, Management of Sex Partners.

Special Considerations

Penicillin Allergy
Data have not been collected systematically for evaluation of therapeutic alternatives to penicillin for treatment of neurosyphilis. Patients who report being allergic to penicillin should either be densensitized to penicillin or be managed

in consultation with an expert. In some situations, skin testing to confirm penicillin allergy may be useful (see Management of Patients Who Have a History of Penicillin Allergy).

Pregnancy
Pregnant patients who are allergic to penicillin should be desensitized, if necessary, and treated with penicillin (see Syphilis During Pregnancy).

HIV Infection
Refer to Syphilis in HIV-Infected Persons.

Syphilis in HIV-Infected Persons

Diagnostic Considerations

Unusual serologic responses have been observed among HIV-infected persons who have syphilis. Most reports involved serologic titers that were higher than expected, but false-negative serologic test results or delayed appearance of seroreactivity also have been reported. Nevertheless, both treponemal and non-treponemal serologic tests for syphilis can be interpreted in the usual manner for most patients who are coinfected with *T. pallidum* and HIV.

When clinical findings suggest that syphilis is present, but serologic tests are nonreactive or unclear, alternative tests (e.g., biopsy of a lesion, darkfield examination, or direct fluorescent antibody staining of lesion material) may be useful.

Neurosyphilis should be considered in the differential diagnosis of neurologic disease in HIV-infected persons.

Treatment

In comparison with HIV-negative patients, HIV-infected patients who have early syphilis may be at increased risk for neurologic complications and may have higher rates of treatment failure with currently recommended regimens. The magnitude of these risks, although not defined precisely, is probably minimal. No treatment regimens for syphilis are demonstrably more effective in preventing neurosyphilis in HIV-infected patients than the syphilis regimens recommended for HIV-negative patients. Careful follow-up after therapy is essential.

Primary and Secondary Syphilis in HIV-Infected Persons

Treatment

Treatment with benzathine penicillin G, 2.4 million units IM, as for HIV-negative patients, is recommended. Some experts recommend additional treatments (e.g., three weekly doses of benzathine penicillin G as suggested for late syphilis) or other supplemental antibiotics in addition to benzathine penicillin G 2.4 million units IM.

Other Management Considerations

CSF abnormalities often occur among both asymptomatic HIV-infected patients in the absence of syphilis and HIV-negative patients who have primary or secondary syphilis. Such abnormalities in HIV-infected patients who have primary or secondary syphilis are of unknown prognostic significance. Most HIV-infected patients respond appropriately to the currently recommended penicillin therapy; however, some experts recommend CSF examination before therapy and modification of treatment accordingly.

Follow-Up

It is important that HIV-infected patients be evaluated clinically and serologically for treatment failure at 3, 6, 9, 12, and 24 months after therapy. Although of unproven benefit, some experts recommend a CSF examination after therapy (i.e., at 6 months).

HIV-infected patients who meet the criteria for treatment failure should be managed the same as HIV-negative patients (i.e., a CSF examination and re-treatment). CSF examination and re-treatment also should be strongly considered for patients whose nontreponemal test titer does not decrease fourfold within 6–12 months. Most experts would retreat

patients with 7.2 million units of benzathine penicillin G (administered as three weekly doses of 2.4 million units each) if CSF examinations are normal.

Special Considerations

Penicillin Allergy
Penicillin-allergic patients who have primary or secondary syphilis and HIV infection should be managed according to the recommendations for penicillin-allergic HIV-negative patients.

Latent Syphilis in HIV-Infected Persons

Diagnostic Considerations

HIV-infected patients who have early latent syphilis should be managed and treated according to the recommendations for HIV-negative patients who have primary and secondary syphilis.

HIV-infected patients who have either late latent syphilis or syphilis of unknown duration should have a CSF examination before treatment.

Treatment

A patient with late latent syphilis or syphilis of unknown duration and a normal CSF examination can be treated with 7.2 million units of benzathine penicillin G (as three weekly doses of 2.4 million units each). Patients who have CSF consistent with neurosyphilis should be treated and managed as described for neurosyphilis (see Neurosyphilis).

Follow-Up

Patients should be evaluated clinically and serologically at 6, 12, 18, and 24 months after therapy. If, at any time, clinical symptoms develop or nontreponemal titers rise fourfold, a repeat CSF examination should be performed and treatment administered accordingly. If between 12 and 24 months the nontreponemal titer fails to decline fourfold, the CSF examination should be repeated, and treatment administered accordingly.

Special Considerations

Penicillin Allergy
Penicillin regimens should be used to treat all stages of syphilis in HIV-infected patients. Skin testing to confirm penicillin allergy may be used (see Management of Patients Who Have a History of Penicillin Allergy). Patients may be desensitized, then treated with penicillin.

Syphilis During Pregnancy

All women should be screened serologically for syphilis during the early stages of pregnancy. In populations in which utilization of prenatal care is not optimal, RPR-card test screening and treatment (i.e., if the RPR-card test is reactive) should be performed at the time a pregnancy is diagnosed. For communities and populations in which the prevalence of syphilis is high or for patients at high risk, serologic testing should be performed twice during the third trimester, at 28 weeks of gestation and at delivery. (Some states mandate screening at delivery for all women.) Any woman who delivers a stillborn infant after 20 weeks of gestation should be tested for syphilis. No infant should leave the hospital without the maternal serologic status having been determined at least once during pregnancy.

Diagnostic Considerations

Seropositive pregnant women should be considered infected unless an adequate treatment history is documented clearly in the medical records and sequential serologic antibody titers have declined.

Treatment

Penicillin is effective for preventing maternal transmission to the fetus and for treating fetal-established infection. Evidence is insufficient to determine whether the specific, recommended penicillin regimens are optimal.

Recommended Regimens

Treatment during pregnancy should be the penicillin regimen appropriate for the stage of syphilis.

Other Management Considerations

Some experts recommend additional therapy in some settings. A second dose of benzathine penicillin 2.4 million units IM may be administered 1 week after the initial dose for women who have primary, secondary, or early latent syphilis. Ultrasonographic signs of fetal syphilis (i.e., hepatomegaly and hydrops) indicate a greater risk for fetal treatment failure; such cases should be managed in consultation with obstetric specialists.

Women treated for syphilis during the second half of pregnancy are at risk for premature labor and/or fetal distress if the treatment precipitates the Jarisch-Herxheimer reaction. These women should be advised to seek obstetric attention after treatment if they notice any contractions or decrease in fetal movements. Stillbirth is a rare complication of treatment, but concern for this complication should not delay necessary treatment. All patients who have syphilis should be offered testing for HIV infection.

Follow-Up

Coordinated prenatal care and treatment follow-up are important, and syphilis case management may help facilitate prenatal enrollment. Serologic titers should be repeated in the third trimester and at delivery. Serologic titers may be checked monthly in women at high risk for reinfection or in geographic areas in which the prevalence of syphilis is high. The clinical and antibody response should be appropriate for the stage of disease. Most women will deliver before their serologic response to treatment can be assessed definitively.

Management of Sex Partners

Refer to General Principles, Management of Sex Partners.

Special Considerations

Penicillin Allergy

There are no proven alternatives to penicillin for treatment of syphilis during pregnancy. Pregnant women who have a history of penicillin allergy should be desensitized and treated with penicillin. Skin testing may be helpful (see Management of Patients Who Have a History of Penicillin Allergy).

Tetracycline and doxycycline usually are not used during pregnancy. Erythromycin should not be used, because it does not reliably cure an infected fetus. Data are insufficient to recommend azithromycin or ceftriaxone.

HIV Infection

Refer to Syphilis in HIV-Infected Persons.

CONGENITAL SYPHILIS

Effective prevention and detection of congenital syphilis depends on the identification of syphilis in pregnant women and, therefore, on the routine serologic screening of pregnant women at the time of the first prenatal visit. Serologic testing and a sexual history also should be obtained at 28 weeks of gestation and at delivery in communities and populations in which the risk for congenital syphilis is high. Moreover, as part of the management of pregnant women who have syphilis, information concerning treatment of sex partners should be obtained in order to assess possible maternal reinfection. All pregnant women who have syphilis should be tested for HIV infection.

Routine screening of newborn sera or umbilical cord blood is not recommended. Serologic testing of the mother's serum is preferred to testing infant serum, because the serologic tests performed on infant serum can be nonreactive if the mother's serologic test result is of low titer or if the mother was infected late in pregnancy. No infant should leave the hospital without the maternal serologic status having been documented at least once during pregnancy.

Evaluation and Treatment of Infants During the First Month of Life

Diagnostic Considerations

The diagnosis of congenital syphilis is complicated by the transplacental transfer of maternal nontreponemal and treponemal IgG antibodies to the fetus. This transfer of antibodies makes the interpretation of reactive serologic tests for syphilis in infants difficult. Treatment decisions often must be made based on a) identification of syphilis in the mother; b) adequacy of maternal treatment; c) presence of clinical, laboratory, or radiographic evidence of syphilis in the infant; and d) comparison of the infant's nontreponemal serologic test results with those of the mother.

Who Should Be Evaluated

All infants born to seroreactive mothers should be evaluated with a quantitative nontreponemal serologic test (RPR or VDRL) performed on infant serum (i.e., umbilical cord blood might be contaminated with maternal blood and might yield a false-positive result). A treponemal test (i.e., MHA-TP or FTA-ABS) of a newborn's serum is not necessary.

Evaluation

All infants born to women who have reactive serologic tests for syphilis should be examined thoroughly for evidence of congenital syphilis (e.g., nonimmune hydrops, jaundice, hepatosplenomegaly, rhinitis, skin rash, and/or pseudoparalysis of an extremity). Pathologic examination of the placenta or umbilical cord using specific fluorescent antitreponemal antibody staining is suggested. Darkfield microscopic examination or direct fluorescent antibody staining of suspicious lesions or body fluids (e.g., nasal discharge) also should be performed.

Further evaluation of the infant is dependent on a) whether any abnormalities are present on physical examination, b) maternal treatment history, c) stage of infection at the time of treatment, and d) comparison of maternal (at delivery) and infant nontreponemal titers utilizing the same test and preferably the same laboratory.

Treatment

Infants should be treated for presumed congenital syphilis if they were born to mothers who met any of the following criteria:

- Had untreated syphilis at delivery;*
- Had serologic evidence of relapse or reinfection after treatment (i.e., a fourfold or greater increase in nontreponemal antibody titer);
- Was treated with erythromycin or other nonpenicillin regimen for syphilis during pregnancy;**
- Was treated for syphilis ≤1 month before delivery;
- Did not have a well-documented history of treatment for syphilis;
- Was treated for early syphilis during pregnancy with the appropriate penicillin regimen, but nontreponemal antibody titers did not decrease at least fourfold; or
- Was treated appropriately before pregnancy but had insufficient serologic follow-up to ensure an adequate treatment response and lack of current infection (i.e., an appropriate response includes a] at least a fourfold decrease in nontreponemal antibody titers for patients treated for early syphilis and b] stable or declining nontreponemal titers of ≤1:4 for other patients).

  Regardless of a maternal history of infection with *T. pallidum* or treatment for syphilis, the evaluation should include the following tests if the infant has either

  a) an abnormal physical examination that is consistent with congenital syphilis,

  b) a serum quantitative nontreponemal serologic titer that is fourfold greater than the mother's titer, or

  c) a positive darkfield or fluorescent antibody test of body fluid(s).

- CSF analysis for VDRL, cell count, and protein;
- Complete blood count (CBC) and differential CBC and platelet count;
- Other tests as clinically indicated (e.g., long-bone radiographs, chest radiograph, liver-function tests, cranial ultrasound, ophthalmologic examination, and auditory brainstem response).

* A woman treated with a regimen other than those recommended in these guidelines for treatment of syphilis should be considered untreated.
** The absence of a fourfold greater titer for an infant does not exclude congenital syphilis.

Recommended Regimens

Aqueous crystalline penicillin G 100,000–150,000 units/kg/day, administered as 50,000 units/kg/dose IV every 12 hours during the first 7 days of life, and every 8 hours thereafter for a total of 10 days;

OR

Procaine penicillin G 50,000 units/kg/dose IM a day in a single dose for 10 days.

If >1 day of therapy is missed, the entire course should be restarted. Data are insufficient regarding the use of other antimicrobial agents (e.g., ampicillin). When possible, a full 10-day course of penicillin is preferred. The use of agents other than penicillin requires close serologic follow-up to assess adequacy of therapy.

In all other situations, the maternal history of infection with *T. pallidum* and treatment for syphilis must be considered when evaluating and treating the infant. For infants who have a normal physical examination and a serum quantitative non-treponemal serologic titer the same or less than fourfold the maternal titer, the evaluation depends on the maternal treatment history and stage of infection.

- The infant should receive the following treatment if a) the maternal treatment was not given, was undocumented, was a nonpenicillin regimen, or was administered ≤4 weeks before delivery; b) the adequacy of maternal treatment for early syphilis cannot be evaluated because the nontreponemal serologic titer has not decreased fourfold; or c) relapse or reinfection is suspected because of a fourfold increase in maternal nontreponemal serologic titer.
  a. Aqueous penicillin G or procaine penicillin G for 10 days. Some experts prefer this therapy if the mother has untreated early syphilis at delivery. A complete evaluation is unnecessary if 10 days of parenteral therapy is given. However such evaluation may be useful; a lumbar puncture may document CSF abnormalities that would prompt close follow-up.[†] Other tests (e.g., CBC and platelet count and bone radiographs) may be performed to further support a diagnosis of congenital syphilis; or
  b. Benzathine penicillin G 50,000 units/kg (single dose IM) if the infant's evaluation (i.e., CSF examination, long-bone radiographs, and CBC with platelets) is normal and follow-up is certain. If any part of the infant's evaluation is abnormal or not done, or the CSF analysis is uninterpretable secondary to contamination with blood, then a 10-day course of penicillin (see preceding paragraph) is required.[††]
- Evaluation is unnecessary if the maternal treatment a) was during pregnancy, appropriate for the stage of infection, and >4 weeks before delivery; b) was for early syphilis and the nontreponemal serologic titers decreased fourfold after appropriate therapy; or c) was for late latent infection, the nontreponemal titers remained stable and low, and there is no evidence of maternal reinfection or relapse. A single dose of benzathine penicillin G 50,000 units/kg IM should be administered. (Note: Some experts would not treat the infant but would provide close serologic follow-up.) Furthermore, in these situations, if the infant's non-treponemal test is nonreactive, no treatment is necessary.
- Evaluation and treatment are unnecessary if the maternal treatment was before pregnancy, after which the mother was evaluated multiple times, and the nontreponemal serologic titer remained low and stable before and during pregnancy and at delivery (VDRL ≤1:2; RPR ≤1:4). Some experts would treat with benzathine penicillin G 50,000 units/kg as a single IM injection, particularly if follow-up is uncertain.

Evaluation and Treatment of Older Infants and Children Who Have Congenital Syphilis

Children who are identified as having reactive serologic tests for syphilis after the neonatal period (i.e., at >1 month of age) should have maternal serology and records reviewed to assess whether the child has congenital or acquired syphilis (for acquired syphilis, see Primary and Secondary Syphilis and Latent Syphilis). If the child possibly has congenital syphilis, the child should be evaluated fully (i.e., a CSF examination for cell count, protein, and VDRL [abnormal CSF evaluation includes a reactive VDRL test, >5 WBCs/mm ^{3} , and/or protein >40 mg/dL]; an eye examination; and other tests such as long-bone radiographs, CBC, platelet count, and auditory brainstem response as indicated clinically). Any child who possibly has congenital syphilis or who has neurologic involvement should be treated with aqueous crystalline penicillin G, 200,000–300,000 units/kg/day IV (administered as 50,000 units/kg every 4–6 hours) for 10 days.

[†] CSF test results obtained during the neonatal period can be difficult to interpret; normal values differ by gestational age and are higher in preterm infants. Values as high as 25 white blood cells (WBCs)/mm^3 and/or protein of 150 mg/dL might occur among normal neonates; some experts, however, recommend that lower values (i.e., 5 WBCs/mm^3 and protein of 40 mg/dL) be considered the upper limits of normal. Other causes of elevated values also should be considered when an infant is being evaluated for congenital syphilis.

[††] If the infant's nontreponemal test is nonreactive and the likelihood of the infant being infected is low, some experts recommend no evaluation but treatment of the infant with a single IM dose of benzathine penicillin G 50,000 units/kg for possible incubating syphilis, after which the infant should have close serologic follow-up.

Follow-Up

All seroreactive infants (or an infant whose mother was seroreactive at delivery) should receive careful follow-up examinations and serologic testing (i.e., a nontreponemal test) every 2–3 months until the test becomes nonreactive or the titer has decreased fourfold. Nontreponemal antibody titers should decline by 3 months of age and should be nonreactive by 6 months of age if the infant was not infected (i.e., if the reactive test result was caused by passive transfer of maternal IgG antibody) or was infected but adequately treated. The serologic response after therapy may be slower for infants treated after the neonatal period. If these titers are stable or increasing after 6–12 months of age, the child should be evaluated, including a CSF examination, and treated with a 10-day course of parenteral penicillin G.

Treponemal tests should not be used to evaluate treatment response because the results for an infected child can remain positive despite effective therapy. Passively transferred maternal treponemal antibodies could be present in an infant until age 15 months. A reactive treponemal test after age 18 months is diagnostic of congenital syphilis. If the nontreponemal test is nonreactive at this time, no further evaluation or treatment is necessary. If the nontreponemal test is reactive at age 18 months, the infant should be fully (re)evaluated and treated for congenital syphilis.

Infants whose initial CSF evaluation is abnormal should undergo a repeat lumbar puncture approximately every 6 months until the results are normal. A reactive CSF VDRL test or abnormal CSF indices that cannot be attributed to other ongoing illness requires re-treatment for possible neurosyphilis.

Follow-up of children treated for congenital syphilis after the newborn period should be the same as that prescribed for congenital syphilis among neonates.

Special Considerations

Penicillin Allergy

Infants and children who require treatment for syphilis but who have a history of penicillin allergy or develop an allergic reaction presumed secondary to penicillin should be desensitized, if necessary, and treated with penicillin. Skin testing may be helpful in some patients and settings (see Management of Patients Who Have a History of Penicillin Allergy). Data are insufficient regarding the use of other antimicrobial agents (e.g., ceftriaxone); if a nonpenicillin agent is used, close serologic and CSF follow-up is indicated.

HIV Infection

Data are insufficient regarding whether infants who have congenital syphilis and whose mothers are coinfected with HIV require different evaluation, therapy, or follow-up for syphilis than is recommended for all infants.

Medical providers play a vital role in the prevention and control of sexually transmitted diseases (STDs). Providers can help significantly reduce the occurrence of these diseases by:

- Evaluating each patient, as appropriate, for evidence of STDs, and for evidence of high-risk sexual behaviors.
- Promptly diagnosing and treating patients with STDs according to current guidelines.
- Providing appropriate follow-up after patients have been treated.
- Providing education and counseling to patients engaging in high-risk sexual behaviors.
- Promptly reporting, as required by Missouri law, all cases of chlamydial infection, gonorrhea, syphilis, and hepatitis B to the local health department, or to the Missouri Department of Health (DOH) at (573) 751-6463. Reports of cases of HIV infection/AIDS should be made as follows:
  - Health care providers in St. Louis City and St. Louis County should report the individual to the St. Louis City Department of Health and Hospitals at (314) 658-1159.
  - Providers in the five-county Kansas City metropolitan area should report to the Kansas City Health Department at (816) 983-4200.
  - All other providers should report to DOH's Office of Surveillance at (573) 751-6463.

Updated Recommendations for Management of Occupational Exposure to HIV

The U.S. Public Health Service has updated its recommendations for the management of health-care workers who have occupational exposure to blood and other body fluids that may contain HIV. (CDC. Public Health Service guidelines for the management of health-care worker exposures to HIV and recommendations for postexposure prophylaxis. MMWR 1998; 47[No. RR-7].) These new guidelines are available on the World Wide Web at: http://www.cdc.gov/epo/mmwr/mmwr_rr.html.

Occupational exposures should be considered urgent medical concerns to ensure timely administration of post-exposure prophylaxis as appropriate. All physician's offices, clinics, hospitals, and other health care facilities should have written protocols in place for the management of such exposures.

State Public Health Laboratory Report

Newborn Screening — Hypothyroidism, Phenylketonuria, Galactosemia and Hemoglobinopathies

James Baumgartner, B.S., M.B.A., Chief, Metabolic Disease Unit

	Nov 97	Dec 97	Total YTD
Specimens Tested	7,619	9,351	113,934
Initial (percent)	73.2%	77.1%	76,810
Repeat (percent)	26.8%	22.9%	37,124
Specimens: Unsatisfactory	80	114	1,984
HT Borderline	719	1,120	10,411
HT Presumptive	22	33	260
PKU Borderline	0	3	8
PKU Presumptive Positive	0	1	9
GAL Borderline	2	4	301
GAL Presumptive Positive	1	2	36
FAS (Sickle cell trait)	81	94	977
FAC (Hb C trait)	18	20	264
FAX (Hb variant)	12	19	173
FS (Sickle cell disease)	2	5	29
FSC (Sickle C disease)	0	2	13
FC (Hb C disease)	0	0	4

HT = Hypothyroidism, PKU = Phenylketonuria, GAL = Galactosemia, Hb = Hemoglobin, YTD = Year to Date

LATE BREAKERS

☞ Lead poisoning continues to be a problem in Missouri. Treating a child with an elevated blood lead level can increase the lead level IF the child's home (or environment) has not been both inspected and remedied, or, the child has not been removed from the environment until remediation has been performed. Chelation therapy causes lead to be absorbed at an increased rate and can result in a higher lead level than the initial one if the patient continues to be exposed to a lead source. This issue is particularly important when using oral chelating agents, administered on an out-patient basis. To arrange for a lead inspection, call your local health department or the Lead Program at (800) 575-9267. It is crucial to immediately report an elevated blood lead level >9mg/dl.

☞ A surveillance project for meningococcal disease and varicella on college campuses is being conducted by the American College Health Association (ACHA) with technical consultation from the Centers for Disease Control and Prevention. The goals of the project are to determine if college students in the United States are at increased risk for meningococcal disease and identify groups at highest risk, and to determine the occurrence, characteristics and clinical profile of varicella and herpes zoster among college students. Results will be utilized in review of recommendations for use of meningococcal and varicella vaccines among college students. During the week of April 12, packets were sent to approximately 1,600 colleges affiliated with ACHA. For more information, contact Georgia Storm in the Bureau of Immunization at (800) 699-2313.

Recommendations for Immunization of Health-Care Workers

In the December 26, 1997 issue of the Centers for Disease Control and Prevention Weekly Morbidity and Mortality Report (MMWR), RR-18, the Advisory Committee on Immunization Practices (ACIP) and the Hospital Infection Control Practices Advisory Committee (HICPAC) published new recommendations for the immunization of health-care workers (HCWs). These recommendations can assist hospital administrators, infection control practitioners, employee health physicians and HCWs in optimizing infection prevention and control programs. Recommendation for administration of vaccines and other immunobiologic agents to HCWs are organized in three broad disease categories:

- Those for which active immunization is strongly recommended because of special risks for HCWs (i.e., hepatitis B, influenza, measles, mumps, rubella and varicella)
- Those for which active and/or passive immunization may be indicated in certain circumstances (i.e., tuberculosis, hepatitis A, meningococcal disease) or in the future (i.e., pertussis); and
- Those for which immunization of all adults is recommended (i.e., tetanus, diphtheria and pneumococcal disease).

Information on immunizing immunocompromised HCWs, postexposure prophylaxis and work restrictions are also included in the recommendations.

If you have questions about immunizations for health-care workers, or would like a copy of the recommendations, please call the Bureau of Immunization at (800) 699-2313.

A copy of the recommendations is also available through the Centers for Disease Control and Prevention Internet Home Page at **http://www.cdc.gov/epo/mmwr/preview/ind97_rr.html**.

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Tuberculosis Testing Project in Charleston, MO

Lynn Tennison, R.N.
Vic Tomlinson
Bureau of Tuberculosis Control

The Charleston Tuberculosis Testing Project was initiated on November 26, 1997 due to the large number of active tuberculosis (TB) cases that had occurred in a particular section of Charleston, MO since 1981, and the large number of reported TB infections without disease that had occurred in the same section of Charleston since 1991. See sidebar and Figure 1.

Tuberculosis in Charleston, MO

Active Tuberculosis	Tuberculosis Infection
1981–97	**1991*–97**
30 Cases	39 Reports
Southwest Charleston	**Southwest Charleston**
70% (21/30) Live in SW	74% (29/39) Live in SW
13 Male/8 Female	15 Male/14 Female
21 African American/0 White	29 African American/0 White
18 Age 25–44	19 Age 25–44

*Tuberculosis infections have only been reportable in Missouri since 1991.

The main concern was that most of the cases were occurring in the southwest area of Charleston. The TB disease case rate for that area was 35/100,000 persons, which is more than seven times the state rate. For this reason, the Mississippi County Health Department and the Missouri Department of Health (DOH) approached the community about organizing a skin-testing initiative to identify individuals who might be transmitting tuberculosis, and to prevent people from developing active disease.

The proposal for the TB skin testing was first presented to the Mississippi County Board of Health for their endorsement. Then the TB problem was discussed with additional community leaders to make them aware of the problem in their community. The community leaders of the Charleston Ministerial Alliance played a key role in educating the community about tuberculosis. Initially, the ministers requested 500 flyers to be inserted into church bulletins. The flyer contained educational information about tuberculosis and the TB testing project to be conducted on January 6, 1998. After the flyers were distributed in the church bulletins, DOH staff met with volunteers. At the meetings, volunteers chose the area they would work in and then DOH staff trained them to perform that particular job.

Fourteen volunteers went door-to-door in the southwest community on the Saturday before the testing date. They talked with people about the testing project and handed out flyers as reminders. From New Year's Eve through the weekend of the testing, a local supermarket, Wal-Mart and a local liquor store placed the flyers in grocery bags. TB posters were placed in stores and public offices along with a flyer announcing the skin-testing project. Media coverage played a key part in the success of the project. Both of the local newspapers carried front-page articles and ran ads about the testing project.

The skin testing was conducted on Tuesday, January 6, 1998 from 9:00 a.m. to 1:00 p.m. and again from 5:00 p.m. to 8:00 p.m. at the Helen Currin Community Center located in southwest Charleston. A total of 264 individuals were tested. Skin test results were read on Thursday, January 8, 1998 at the same location and during the same time period. A total of 245 individuals (92.8% of those tested) returned to have the test results read, and of that number 32 (13%) were positive.

A total of 30 volunteers and local and district health agency staff helped with the skin testing on January 6. Volunteers provided assistance by completing paperwork on those who were tested, serving refreshments and providing transportation to and from the testing site. They also continued to talk with people in the community to make them aware of the testing project. On January 8, when the skin test results were read, volunteers again provided transportation, assisted with paperwork and handed out restaurant coupons. They also called people to remind them to come back to have their test results read.

Incentives were used to encourage people to participate in the skin testing and to return to have their test results read. The incentives included refreshments, such as cookies and punch, served the day of the testing, and $2.00 restaurant coupons given out when they returned to have their test read.

No cases of active tuberculosis disease were discovered as a result of the skin testing project. However, 32 people were found to have a positive (reactive) skin test. After questioning, we were able to determine that nine (28.1%) of these individuals had positive skin tests in the past, and four of the nine had received INH preventive therapy. Six (18.8%) of those with positive skin tests were found to be contacts to a person who had been diagnosed with tuberculosis within the past nine months.

Using Centers for Disease Control and Prevention guidelines, twelve (37.5%)

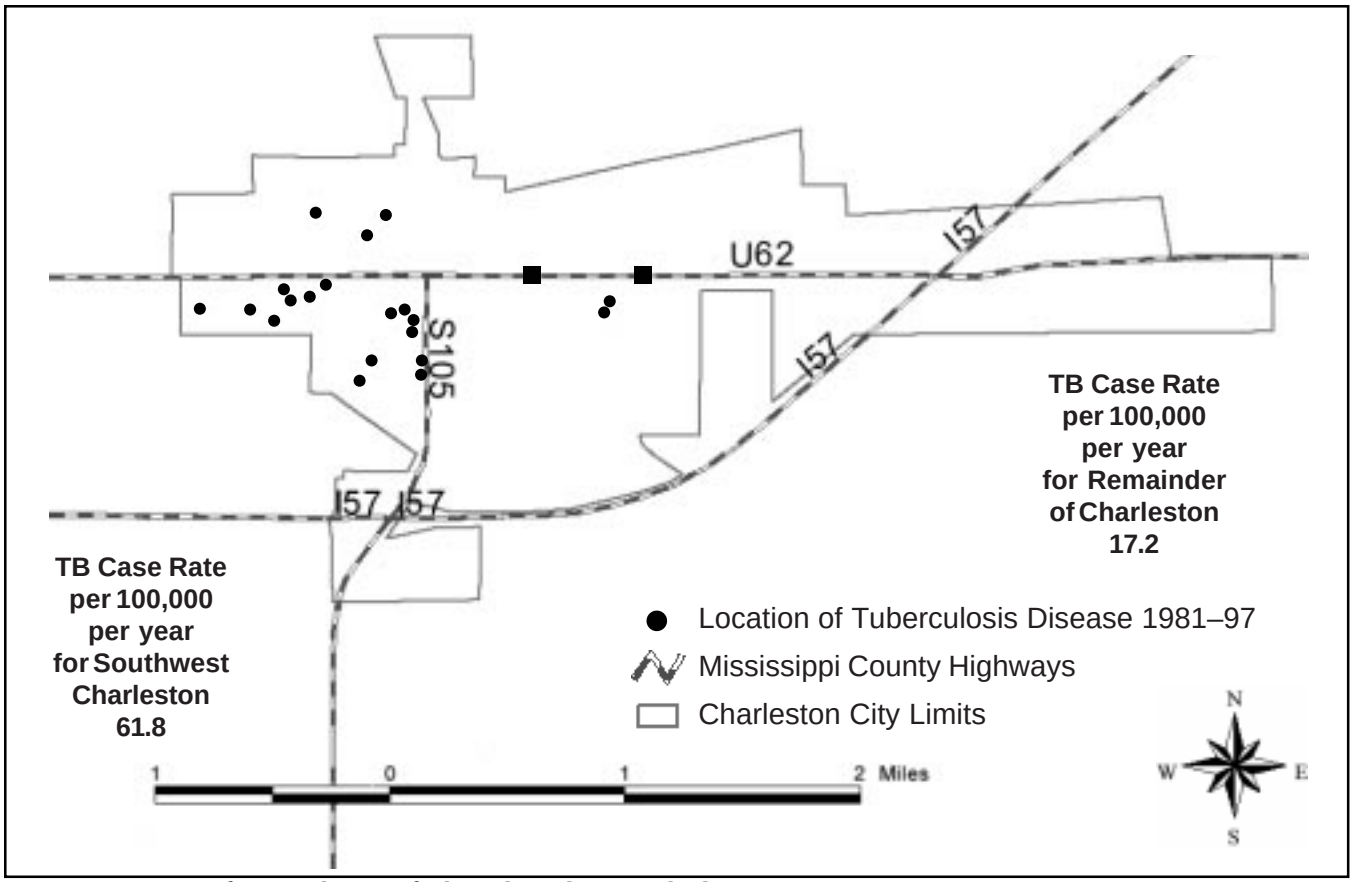

Figure 1. Location of reported cases of tuberculosis disease, Charleston, Missouri, 1981–1997.

individuals were determined to be at high risk for developing active tuberculosis and were started on preventive therapy. DOH staff will be working with volunteers in the community to do directly observed preventive therapy (DOPT) for those individuals.

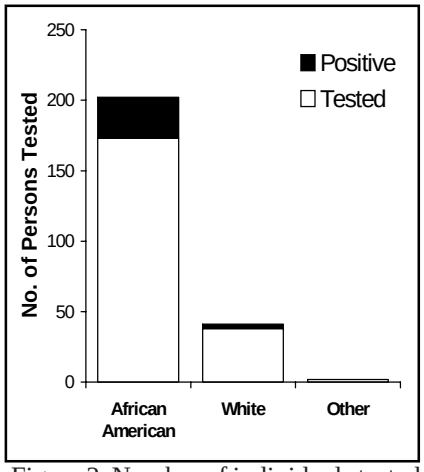

Figure 2. Number of individuals tested and positive by race, Charleston TB Testing Project, Missouri, 1998.

There were 9.4% more women skin tested than men. The majority (82.4%) of those tested were African Americans. See Figure 2. The highest rates of positive reactors were in the 25–44 and ≥65 years age groups, 31.3% and 37.5% respectively. See Figure 3.

In summary, many individuals, both volunteers and public health agency staff, worked together to make this skin testing project a success. Community members played a key role in mobilizing the citizens to take action. Without their involvement and commitment, this project would not have been a success. This project is an excellent example of what can be accomplished to achieve a common goal when the Department of Health, a local public health agency and the citizens of a community work together. Other local agencies, businesses and the local press were all a great asset and also contributed to the success of the project.

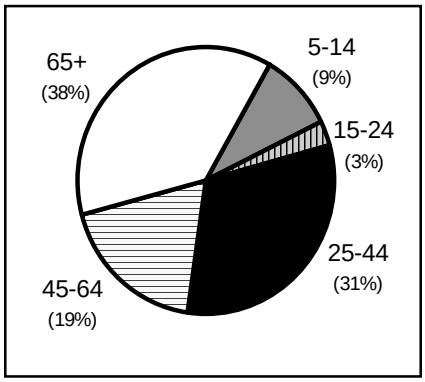

Figure 3. Number positive reactors tested by age group, Charleston TB Testing Project, Missouri, 1998.

We thank Dr. Robert Hamm for his assistance in analyzing the data from the Charleston TB Testing Project.

Heat Surveillance Summary - 1997

Diane C. Rackers
Office of Epidemiology

The summer of 1997 was relatively normal for Missouri with one peak of high heat indexes from July 12 through July 28. The Department of Health issued the only statewide Hot Weather Health Advisory for the summer on July 25 when heat indexes reached 112º in St. Louis, 110º in Kansas City, 108º in Columbia and 105º in Cape Girardeau. The peak of high heat indexes from July 12 through July 28 accounted for 76% (176) of the heat-related illnesses reported in 1997. See Figure 1.

In 1996, one statewide Heat Warning and one statewide Heat Alert were issued. This would be comparable to one Hot Weather Health Advisory and one Hot Weather Health Warning; new terms for heat advisories were adopted in 1997. See sidebar on page 31 for new terms.

In 1997, a total of 232 heat-related illnesses was reported. This is higher than the 198 heat-related illnesses reported in 1996, but considerably lower than the 819 heat-related illnesses reported in 1995. See Figure 2.

In 1997, nine heat-related deaths were recorded. This is two more deaths than reported in 1996, but considerably lower than the 57 heat-related deaths reported in 1995. See Figure 3. Eight (89%) of the heat-related deaths in 1997 were in individuals aged 60 or older.

As in past years, the St. Louis metropolitan area accounted for a large proportion of the heat-related illnesses and deaths in 1997; 126 (54%) of the heat-related illnesses and six (67%) of the heat-related deaths.

St. Louis Operation Weather Survival issued one Hot Weather Health Watch, three Hot Weather Health Advisories and one Hot Weather Health Warning in 1997, all during the high heat index peak from July 12 through July 28. During that time period, St. Louis had 13 days when

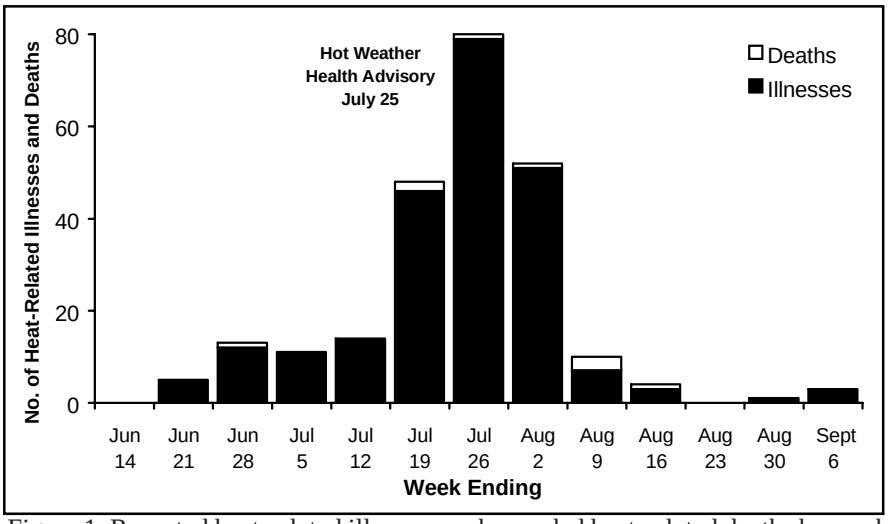

Figure 1. Reported heat-related illnesses and recorded heat-related deaths by week of occurrence, Missouri, Summer 1997.

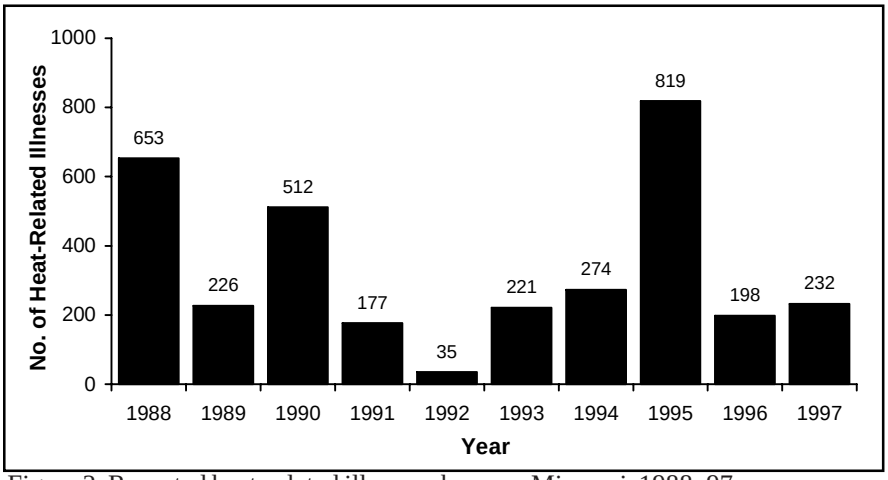

Figure 2. Reported heat-related illnesses by year, Missouri, 1988–97.

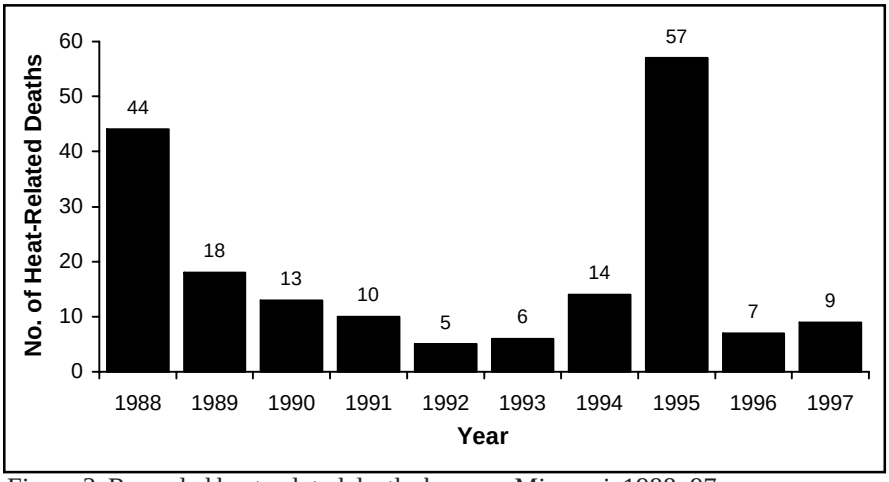

Figure 3. Recorded heat-related deaths by year, Missouri, 1988–97.

the heat index at the St. Louis airport was 100º or higher. We estimate that the heat index in downtown St. Louis during this time period was 105º or higher. Without the diligent efforts of St. Louis Operation Weather Survival the number of heat-related illnesses and deaths in the St. Louis metropolitan area during this time period would very likely have been much higher. This coordinated effort between public health agencies, voluntary organizations, the media and others has been very effective in reducing excess mortality due to stressful weather conditions in the St Louis area.

During periods of high temperatures, physicians, nurses and hospital and nursing home personnel should give special attention to their high risk patients. Attempts should be made to provide air-conditioned environments for such patients. Health care personnel should at least warn such patients regarding their high risk and encourage the drinking of extra non-alcoholic fluids, reduction of activity and close supervision by family, friends or staff, as appropriate.

For patients who have restricted salt or fluid intake, one should consider liberalizing the daily allotments. Weekly or even daily contact with the physician may be necessary. Frequent assessment and reassessment of a patient's fluid and electrolyte status may be highly desirable, especially for those who also are taking diuretics, potassium supplements or other medications which similarly affect electrolyte balance or are affected by changes in electrolyte balance. Routine use of salt tablets is not recommended.

Reemphasize to patients preventive measures to reduce heat-related illness during prolonged hot weather:

- Avoid direct sunlight.
- Stay in coolest location available.
- Spend time in an air-conditioned place.
- Place wet towels or ice bags on the body or dampen clothes.
- Take cool baths or showers frequently.
- Reduce the number of layers of clothing.
- Wear light-weight, loose-fitting garments.
- Avoid strenuous physical activity and reschedule activities, such as shopping, to a cooler time of day.
- Increase intake of fluids such as water and juices.
- Avoid alcoholic beverages (beer, wine or liquor).
- Contact family or friends at least once a day.

Prompt notification of heat-related illnesses and deaths is essential for an effective heat surveillance system. If you are aware of heat-related illnesses or deaths, please report them promptly to your local health department.

Further information on prevention of heat-related illness and past surveillance data for Missouri can be obtained through the Department of Health Home Page at **http://www.health.state.mo.us/cgi-bin/uncgi/HeatRelatedInfo.**

Department of Health
Stages of Hot Weather Health Advisories

A statewide **Hot Weather Health Advisory** will be issued when heat indexes of 105° in a large proportion of the state are first reached (or predicted). The Department of Health will inform the public about the risks of heat-related illness and urge concern for those at high risk. Monitoring of temperatures and heat indexes will be intensified. An **Advisory** will not be canceled.

A statewide **Hot Weather Health Warning** will be issued when:

1. Heat indexes, measured at peak afternoon temperatures, have remained at 105° or more for two days in a large proportion of the state **and**
2. When weather predictions are for continued high-stress conditions for at least 48 hours in a large proportion of the state.

During a **Warning**, the Department of Health will encourage local health departments to assure that cooling shelters are available and also encourage other community agencies to provide relief from the heat stress. A **Warning** will be downgraded or canceled when heat indexes in a large proportion of the state fall below 105° for 48 hours and the forecast is for 48–72 hours of continued relief from heat stress.

The Department of Health will recommend to the Governor that a statewide **Hot Weather Health Emergency** be declared when:

1. Extensive areas of the state are experiencing high and sustained levels of heat stress (determined when the heat index reaches 105° for three days); **and**
2. Surveillance data demonstrate increased levels of heat-related illness and death statewide; **and**
3. The National Weather Service predicts that hot and humid conditions are likely to continue for several days in a large proportion of the state.

An **Emergency** will be canceled when the heat indexes in a large proportion of the state fall below 105° for 48 hours and the National Weather Service predictions indicate a low probability for the return of severe conditions for the following 48 to 72 hours.

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The Managing Editor is H. Denny Donnell, Jr, MD, MPH, State Epidemiologist. Production Manager is Diane C. Rackers. Questions or comments should be directed to (573) 751-6128 or toll free (800) 392-0272.

Alternate forms of this publication for persons with disabilities may be obtained by contacting the Missouri Department of Health, Office of Epidemiology, P.O. Box 570, Jefferson City, MO 65102-0570, Ph: (573) 751-6128. TDD users can access the preceding phone number by calling (800) 735-2966.

Upcoming Conference

THE ESSENTIALS OF INFECTION CONTROL
8TH ANNUAL CONFERENCE

September 16–18, 1998
Capitol Plaza Hotel, Jefferson City, MO

Purpose:
This conference is a **STARTING POINT** to prepare health care professionals as facilitators and resource persons in the prevention and control of common nosocomial infections. It will aid the professional **new to the responsibilities of infection control** to manage the everyday responsibilities of infection surveillance, analysis of disease data, and problem identification and resolution. Important resources for assistance **will also be shared**.

Sponsors:
Missouri Department of Health, Missouri Hospital Association, Missouri APIC Chapters and other organizations.

Registration:
For a complete conference brochure and registration form, call (573) 751-6115.

You Should Attend If You Are A:
Health care professional **NEW** to the field or to the tasks of an infection control professional, or who assists with:

- the infection control program in any health care setting (acute care, ambulatory care, home health, long-term care, mental health, public health, rehabilitation, other)
- consultation on infectious disease prevention and control
- outbreak investigation and follow-up
- surveys, investigations or licensing activities relevant to infection control practices.

Experienced infection control professionals will find day 3 of the conference beneficial.

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